# The British Journal of Surgery

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# PULMONARY ADENOMATOSIS

BY H. E. HUTCHISON AND K. FRASER

FROM THE DEPARTMENT OF PATHOLOGY OF THE UNIVERSITY AND WESTERN INFIRMARY OF GLASGOW, AND THE THORACIC SURGICAL UNIT, HAIRMYRES HOSPITAL, GLASGOW

ADVANCES in thoracic surgical technique in recent years have brought within sight the possibility of cure, by radical excision, of localized forms of malignant disease of the lung. This has stimulated interest in pulmonary neoplasms, one consequence of which has been the intensive study of the rather ill-defined group of so-called alveolar-cell tumours, which includes the condition known as pulmonary adenomatosis.

Alveolar-cell tumours are rare ; the first mention of these neoplasms was made by Malassez as long ago as 1876, the first British case being recorded in the following year (Finlay and Parker, 1877), and yet by 1942 Neubuerger and Geever could find only 25 cases in the world literature, to which they added 2 more. During the last decade, however, the improved prospects of surgical treatment have stimulated interest in these growths and Swan (1949), in presenting 9 cases of his own, found that 26 cases had been published by others since Neubuerger and Geever's review in 1942.

Progressive involvement of the lung substance is usual in untreated cases, but all gradations are met with between highly differentiated tumours of low malignancy apparently amenable to surgical treatment and diffuse carcinomas. Therefore, recognition of this uncommon condition is now of practical therapeutic importance and so the following description of a recent case is presented.

## CASE REPORT

CLINICAL.—The patient was a 36-year old married woman who, six months prior to admission to Hairmyres Hospital, began to be easily tired. The feeling of lassitude persisted and was followed, about a month later, by a sharp attack of what seems to have been pneumonia. This began with a rigor and a bout of coughing productive of frothy sputum ; there was pain in the lower part of the right side of the chest on deep breathing, but later the pain moved to her right shoulder and then became so severe that injections of morphine were necessary to obtain relief. Her sputum was white and frothy and never purulent or blood-stained. She was treated with sulphonamides but made only a partial recovery from this illness, which kept her in bed for four weeks. Four months after the onset of her symptoms she was admitted to the local hospital, where a patchy consolidation of the right lower lobe was found on X-ray examination. In hospital she became worse and, although some improvement followed penicillin treatment, pain and lack of energy persisted and the consolidation of the right lower lobe remained unchanged (*Fig.* 1).

On admission to Hairmyres Hospital on Jan. 2, 1951, her lack of energy was obvious and she was slightly dyspnœic even at rest in bed ; pain, worse on deep breathing, was still present in the right lower chest. There was no cyanosis and no clubbing of the fingers. Respiratory excursion at the right base was reduced and the percussion note was impaired there and in the axilla.

FIG. 1.—Pre-operative radiograph showing diffuse consolidation of right lower lobe. A few poorly-circumscribed opacities are seen in the upper part of the lobe.

Over these areas vocal fremitus and vocal resonance were increased and the respiratory murmur was bronchial ; at one point bronchophony was heard and there were many crepitations at the height of inspiration. Radiographs of the chest showed consolidation of the right lower lobe with probably involvement of the middle lobe.

On Jan. 10 she was bronchoscoped by Dr. T. Semple, who reported : " Trachea and carina normal. Left stem bronchus normal. Right bronchial tree normal except that the right upper-lobe orifice is rather more obvious than normal. There is a continuous flow of clear mucus from the apical segment orifice of the right lower lobe. All the other orifices were dry and normal." She had been having penicillin since admission but without benefit.

AT OPERATION.—On Feb. 13, under pentothal, cyclopropane, and gas and oxygen anæsthesia by Dr. G. Robson, the left bronchus was blocked. The chest was opened through the bed of the seventh rib by Mr. Bruce M. Dick. The upper lobe was found to be free, but the lower and middle lobes were adherent to the chest wall and to the diaphragm. The lower lobe was entirely replaced by a firm carneous mass which was broken into in stripping the lobe off the chest wall and showed an appearance like placental tissue, i.e., in places it was firm and had a papilliferous architecture. In addition, multiple small nodules were observed scattered throughout the middle lobe, particularly in its medial segment, so that it looked as if the disease process had started in the lower portion of the lower lobe and was gradually spreading upwards through the whole lung. No enlargement of the hilar glands was noted. The lower lobe was removed by dissection lobectomy and the chest was closed.

Following operation her progress was satisfactory apart from a massive venous thrombosis of the left leg. This eventually healed and she went home after 10 weeks.

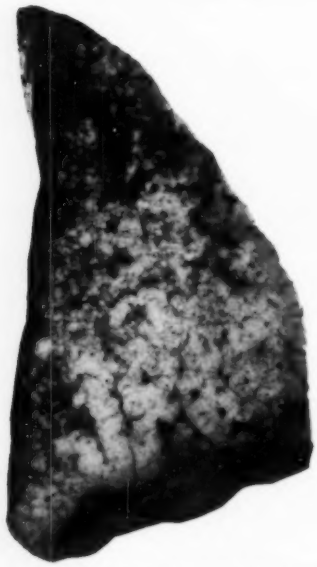

FIG. 2.—The cut surface of the surgical specimen. (× ½.)

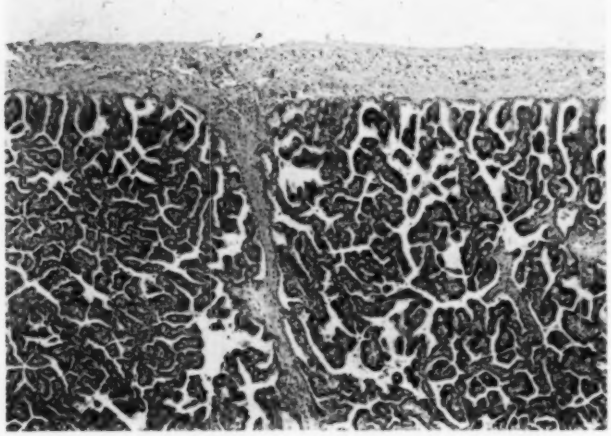

FIG. 4.—Area of confluent tumour showing failure of the neoplasm to invade the pleura or to destroy an interlobular septum. H. and E. (× 37·5.)

THE SPECIMEN.—The gross external appearance of the specimen has been described in the operative findings. On section the major portion of the lower lobe was found to contain pale tumour of a regularly lobulated appearance, but, towards the periphery and in the upper part of the lobe, the neoplasm was present in the form of multiple small nodules. These varied in size from some about 1 cm. in diameter, which from their lobulated outline seemed to have been formed by the coalescence of smaller nodules, through infinite gradations to others so small as to be scarcely discernible by the unaided eye. It will be observed (*Fig.* 2) that the distribution of the growth in the lung follows a pattern and that the nodules are not scattered haphazardly throughout the lobe. This appearance suggests that by the growth and coalescence of these small nodules the more uniform replacement of the lower part of the lobe has been produced, involvement of the lateral and upper parts being more recent. Nowhere is there an obvious relation to larger air-passages as a site of primary origin for the growth. It is noteworthy that even where the tumour is most extensive the lobular markings of the lung are still apparent and that there is no necrosis or evidence of other degenerative change.

On the pleural surfaces both diaphragmatic (*Fig.* 2) and costal (*Fig.* 3) pale areas of tumour show through

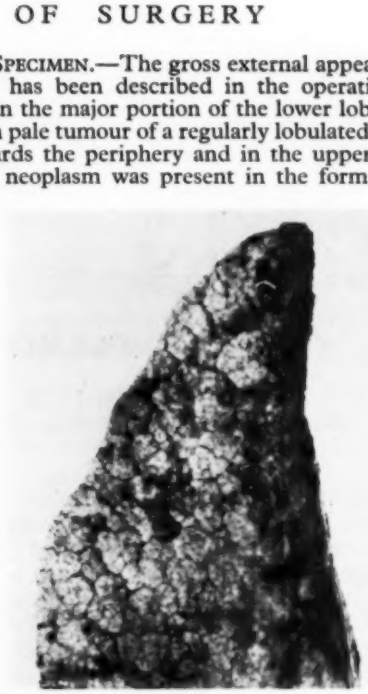

FIG. 3.—The pleural surface of the specimen. (× ½.)

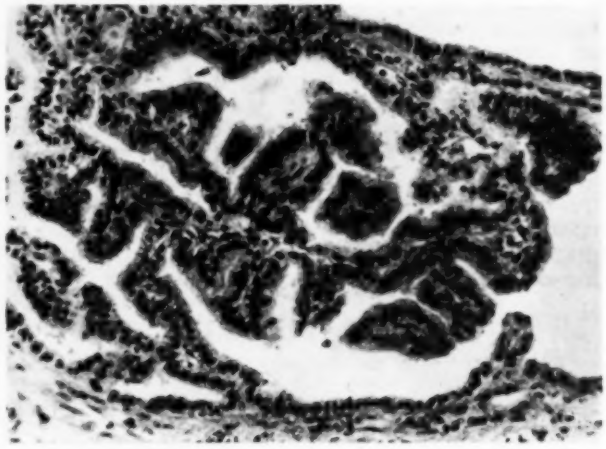

FIG. 5.—The papillary structure of the growth is illustrated both in *Fig.* 4 and in this photograph at higher magnification, when the regular arrangement and general characters of the epithelial cells can also be appreciated. H. and E. (× 217·5.)

the serosa. There is, however, no invasion of the pleural surfaces by the tumour. A few old adhesions are present, and slight recent hæmorrhage is seen, doubtless the result of manipulations during operative removal of the lung.

It is fortunate that the material on which the description of the pathological changes is based was obtained at operation. Because of this the pathological process is

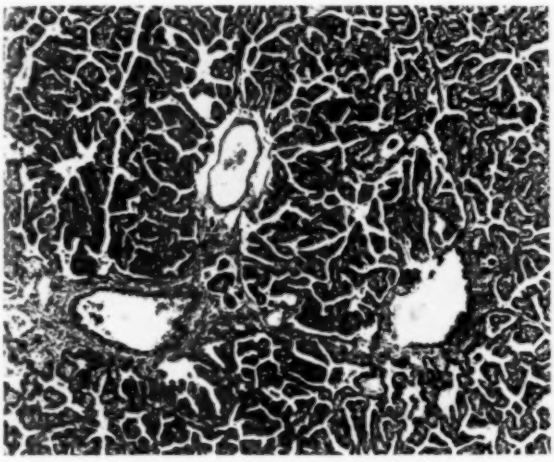

FIG. 6.—Two small bronchioles and a pulmonary vein clearly recognizable in an area of confluent tumour. Note the absence, however, of the alveolar framework of the lung, which appears to have been completely replaced. H. and E. (× 24.)

available for study in a pure form uncomplicated by the presence of secondary infection, which is a common terminal event in the natural history of this disease.

*Pathological Histology.*—On microscopical examination the lung substance in the basal part of the lobe seems at first sight to have been completely replaced by tumour, the most striking architectural feature of which is the papillary structure well shown in *Figs.* 4 and 5. In some places, however, on close examination the alveolar framework can still be recognized, more fibrous than normally, forming the stroma of the growth, but generally this is not so. Although the alveolar pattern is no longer distinguishable in most areas, it is noteworthy that the pleura has not been invaded and that the interlobular septa have also been preserved (*Fig.* 4). Indeed, both these structures are more prominent than normal owing to fibrous thickening. Furthermore, small bronchioles can still be distinguished even in areas which at first sight appear completely replaced by tumour, as in *Fig.* 6. These features indicate that the growth has only a limited power of replacing the normal parenchyma. At higher magnification the tumour cells (*Fig.* 5) are seen to be cubical or low columnar and are arranged with great regularity in a single layer. They are non-ciliated and only occasionally mucin-secreting. The size of the cells varies little ; the cytoplasm is faintly eosinophilic and the rather oval nuclei lie at about the same level, centrally, in each cell and are of uniform fairly dense appearance. Indeed, the uniformity in appearance of the growth in different areas is a striking feature and this applies not only to the individual cells but also to their general arrangement. There is a complete absence of anaplasia, no mitotic figures are observed, and there is no evidence of lymphatic permeation by the tumour cells.

In the upper and more peripheral parts of the lobe the essentially nodular character of the growth is well shown (*Fig.* 7). Here small nodules of tumour lie among lung alveoli which are little altered or show a mild catarrhal reaction ; some contain recently shed blood, the result of operative trauma, but nowhere is a lipophage reaction prominent.

In brief, pathological examination discloses a multiple nodular growth, with areas of confluence, which proves on microscopical investigation to be an epithelial tumour of highly differentiated architecture with only very restricted powers of replacing the lung structure.

SUBSEQUENT COURSE.—Soon after her return home she began to be troubled again by cough, shortness of

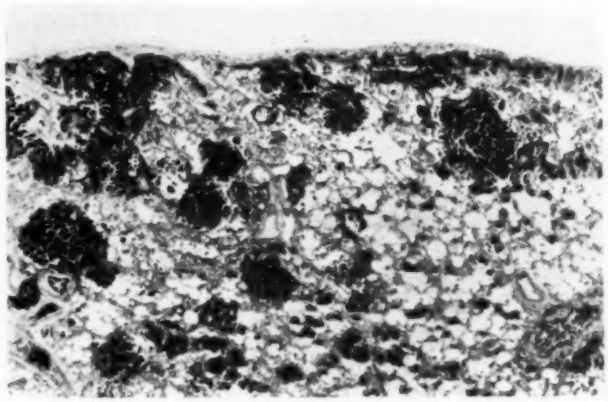

FIG. 7.—From the upper part of the lobe illustrating the multiple nodular distribution of the tumour where involvement of the lung is early. Blood is present in some of the alveoli, presumably the result of operative trauma. H. and E. (× 9.)

breath, and the expectoration of large quantities of frothy sputum. X-ray examination two months after her discharge from hospital (*Fig.* 8) revealed involvement of the remaining portion of the right lung and also small

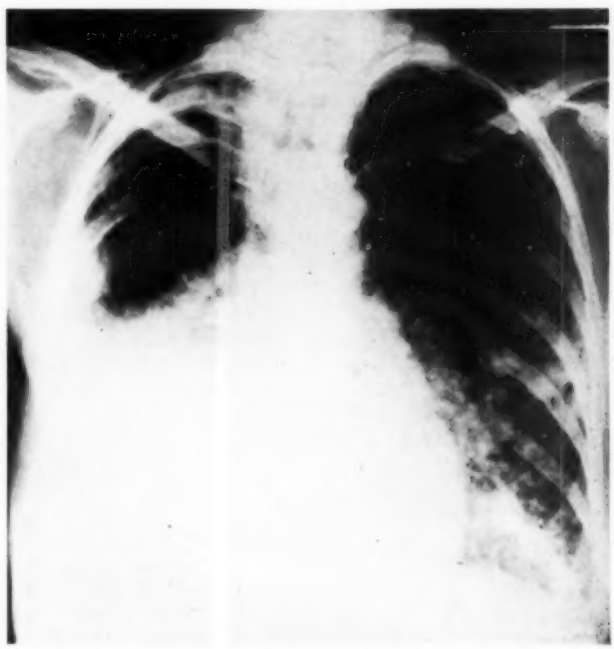

FIG. 8.—Radiograph taken two months after operation, showing spread of the disease in right upper lobe and to left lung. The discrete character of the lesions is well shown.

areas of opacity in the left lung most numerous towards the base. Her general condition had deteriorated and it became steadily worse as time went on. Cough was extremely troublesome and she died at home six months after operation. A necropsy was not obtained.

## DISCUSSION

In presenting this case as one of pulmonary adenomatosis we are conscious that without post-mortem examination to exclude an extrapulmonary site of origin the evidence is incomplete. The anatomical features and the histological characters of the growth are, however, in keeping with the descriptions of pulmonary adenomatosis in the literature, and the absence of evidence of any extra-pulmonary lesion is further support for our belief that the lung was in fact the site of primary origin of the neoplasm. Nevertheless, the multiple nodular character of such growths always demands that consideration should be given to the possibility of spread from an extrapulmonary source, for we have observed examples of secondary pulmonary growths in which the morbid anatomical appearances in the lung resembled closely those of pulmonary adenomatosis. Such an occurrence seems unlikely in the present case when it is recalled that the disease, while extensive in the right lung, was limited to it, so far as could be detected, when the patient first presented; a unilateral distribution would be very improbable in carcinomatosis. Furthermore, the distribution of the disease indicated progressive involvement from the base of the lung to the apex; it was not haphazard, as in blood-borne metastases, and on histological examination of the excised lobe it was clear that the multiple nodules were not the result of dissemination of cancer via the lymphatics. In adenomatosis the multiple nodular character of the growth may, in any case, be accounted for either by seeding within the lung or by the growth being multifocal in origin.

In considering sites of primary origin of cancer from which spread to the lung might have produced histological appearances similar to those found in the case under discussion, the two chief possibilities are ovary and thyroid. Either of these organs could have been the source of a tumour with the papillary structure of this neoplasm while the restricted invasiveness and general absence of cytological evidence of malignancy of the growth would fit particularly well a neoplasm originating primarily in the thyroid on the analogy of the benign metastasizing goitre; but the lung tumour produced mucin and as this is not a feature of thyroid neoplasms it is probably sufficient to exclude the thyroid from further consideration as a possible primary site. The fact that the patient showed no sign of a pelvic disorder is only of limited value in excluding the possibility of ovarian cancer, and the account by Nicholson (1909) of a symptomless ovarian cancer which metastasized widely to the lungs and to no other organ outside the pelvis engenders caution lest the possibility be dismissed without adequate consideration, for these metastases used the alveolar walls as their stroma and so produced an appearance strongly resembling the more highly mucin-secreting varieties of adenomatosis. The even distribution of cases between the sexes in the examples of pulmonary adenomatosis recorded in the literature is, however, clearly against confusion with secondary ovarian carcinoma having been a frequent occurrence, and in the present case the histological features of the growth are not strongly suggestive of secondary ovarian carcinoma. The high degree of differentiation and the corresponding lack of invasiveness are not what one would expect to see in such metastases. Furthermore, there was no evidence on histological examination of lymphatic involvement and, as has been said, the pattern of distribution of the tumour in the lung was clearly against blood-borne metastases. In brief, the case described conforms in every particular with accounts of the pathology of pulmonary adenomatosis in the literature (Weissmann, 1934; Sweany, 1935; Bonne, 1939; Dacie and Hoyle, 1942; Sims, 1943; Drymalski, Thompson, and Sweany, 1948) and presents no features which would suggest an alternative diagnosis.

The clinical features and the natural history of this case are also in keeping with the descriptions of pulmonary adenomatosis given in the literature (Jennings, 1948; McCallum, 1949). The illness lasts usually from six months to two years and it is characterized by steady deterioration in the patient's general condition and aggravated by one or more attacks of pneumonia. The production of abundant clear sputum has been a feature in many and is, indeed, the only symptom of any diagnostic value. Hæmoptysis has occurred in only about one-third of the cases. Physical examination of the chest in the early phase may reveal patchy dullness attributable to areas of consolidation which, on X-ray examination, show as small, poorly-defined shadows. With further progress of the disease dullness may involve an entire lobe and further patches may be found in other lobes, as is confirmed by the X-ray appearances where coalescence of shadows may give rise to a picture like that of an atypical pneumonia or of a mycosis. Consolidation of an entire lung may result and ultimately the opposite lung may become similarly involved. (For details of the radiological changes *see* Geever, Carter, Neubuerger, and Schmidt, 1945; Paul and Ritchie, 1946; Kent, 1951.)

Endoscopic examination frequently fails to reveal any abnormality, but sometimes an excess of serous fluid is seen welling up in the bronchus of the affected lobe. The examination is of value, however, in that it excludes the possibility of a bronchial carcinoma in the stem and medium-sized bronchi, and it also provides the opportunity to obtain a sample of the bronchial secretion for cytological examination. The value of sputum examination, which is more frequently employed in the United States than in this country, seems to be considerable. Thus, Good, McDonald, Clagett, and Griffith (1950) report that the cytological findings suggested the diagnosis in 4 out of the 6 cases in which they employed the method. Cytological examination of sputum from the present case was not carried out until one month after operation and then no abnormality of the cellular constituents was detected.

Pulmonary adenomatosis occurs chiefly between the ages of 40 and 60 years, so it is not surprising that cases are frequently mistaken for carcinoma of the lung, especially when the changes are localized to a single area of opacity or to a single lobe. Undoubtedly pulmonary adenomatosis should be considered in any case in which there is abundant, relatively uninfected, clear frothy sputum, and when the X-ray appearances show progressive consolidation in one lobe or multiple small opacities in one or more lobes. Cytological examination of the sputum may be

helpful; it should certainly be done (Griffith, McDonald, and Clagett, 1950).

In many instances the patchy nature of the consolidation has led to the erroneous diagnosis of bronchopneumonia, and when an entire lobe is involved unresolved pneumonia has to be considered. When the disease becomes widespread advanced tuberculosis or carcinomatosis may be suspected.

The treatment of these cases is a difficult problem. From a study of the literature it is apparent that the disease advances fairly rapidly with progressive involvement of the lung substance, death occurring within a period to be reckoned in months rather than years. This is a strong argument in favour of radical excision when the disease is in the early stage and more and more cases are now receiving surgical treatment. Thus, prior to 1943 only 3 of the cases reported had been treated surgically. In recent years with increasing recognition of the condition and the introduction of more active measures in the investigation and treatment of suspicious radiological opacities, as many as 8 cases have been treated at one centre (Good and others, 1950). The difficulty is to detect the early case; only too often the disease does not declare itself until it has advanced beyond the stage at which complete excision is possible. There is, however, another and more fundamental difficulty; it is undecided as yet whether the disease spreads through the lungs by a process of intrapulmonary seeding or whether it is of multifocal origin in the lung tissue. It is, therefore, uncertain whether the disease will ultimately prove amenable to surgical treatment. On reviewing the cases treated surgically it is found that these have been unilateral and apparently free of metastases to the bronchial nodes, i.e., they are of the less malignant type. When both lungs are involved it is obviously impossible to extirpate the disease by surgical measures and in such cases radiotherapy has usually been employed. The total number of cases recognized during life and treated either surgically or by radiotherapy is, however, insufficient to provide a clear indication of the usefulness of these measures in the management of this rare disease.

'Pulmonary adenomatosis', a term originally used in veterinary pathology to describe a morphologically similar disease in sheep (Dungal, 1938), seems a more appropriate name meantime than 'alveolar-cell tumour' (Neubuerger, 1941) for cases of this kind in view of the uncertainty regarding the precise cell type in the lung from which these neoplasms take origin. It may be argued that this designation suggests a benign lesion whereas the condition was malignant, since by its growth and extension it took the patient's life. Histologically the growth would be classified as only locally malignant, the possibility being that more active growth might develop, especially in those areas where the epithelium was mucin-secreting. In the absence of necropsy we are unable to state whether extrapulmonary metastases ultimately developed and so to that extent we lack precise knowledge, but in this disease, unlike bronchial cancer, metastases are not the most frequent cause of death. Septic complications in the lungs are common in both diseases terminally, but whereas pulmonary insufficiency due to extensive involvement of the lung substance by tumour rarely develops in bronchial cancer, it is common in pulmonary adenomatosis, which frequently kills by the progressive involvement of more and more lung tissue until eventually too little is left to sustain life. Such behaviour is not incompatible with the designation 'adenomatosis'.

## SUMMARY

The clinical and pathological features are described of the first case of pulmonary adenomatosis to be recorded in this country, in which the diagnosis was made before death. The only symptom of diagnostic value was the expectoration of abundant frothy sputum.

The disease was present in the lobectomy specimen in the form of multiple nodules which had coalesced to produce almost uniform involvement of the lower and medial part of the lobe. There was no invasion of the pleura and microscopical examination disclosed a highly differentiated epithelial neoplasm of pronounced papillary architecture and only very restricted powers of replacing the normal lung structures. Mucin formation was not a pronounced feature of the growth.

After operation the remaining portion of the right lung became involved and the disease spread also to the left lung. The patient became progressively more dyspnœic and died at home six months after operation. A necropsy was not obtained.

The differential diagnosis is discussed from both clinical and pathological aspects, and mention is made of the features of the disease which render the designation 'pulmonary adenomatosis' appropriate to such cases.

We wish to express our thanks to Mr. Bruce M. Dick for permission to publish this case and to Mr. W. Penny, F.I.M.L.T., for his work in the preparation of the histological sections.

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# GALL-STONE ILEUS

By P. J. M. WRIGHT and P. A. TRAFFORD, Aldershot

This article presents a brief summary of the literature (about 600 cases) together with a report of 3 cases of our own.

**Statistics.**—The incidence of gall-stone ileus is reported as between 0·7 and 2·5 per cent of all cases of intestinal obstruction. The site at which obstruction occurs is in the terminal ileum in 85 per cent of cases. The difficulty of calculation of these figures arises from the fact that spontaneous relief may occur, and, since the number of such cases is extremely difficult to assess, any figures must be fallacious. The mortality of biliary ileus may be as high as 70 per cent. It is possible that in the future reduction both of incidence and mortality may occur by reason of the increasing practice of cholecystectomy and of the use of modern methods in the treatment of intestinal obstruction.

**History, Signs, and Symptoms.**—The patient is usually an elderly, obese, flatulent female and the sex incidence of biliary ileus is very much the same as that of cholecystitis, namely, seven females to one male. In the past history it is found that some 15 per cent of the patients have always had good health with no previous dyspepsia, 10 per cent have had jaundice, and the remainder varying degrees of ill health. Flatulent dyspepsia is said to be common. There may be a history of previous attacks of subacute intestinal obstruction. Constipation is an unreliable symptom, as only 20 per cent of the patients have a complete obstruction, and the higher the obstruction the less likely is constipation to be a predominant feature. On the other hand, fæculent vomiting will occur earlier. It is possible that silent stones may exist in the alimentary tract, having been passed months or years previously either by fistula or by the natural passages, and they may come to rest in the large intestine and there acquire successive layers of fæcal or similar material until such time as obstruction occurs. Support is lent to this theory by the fact that some stones found in the large intestine could not possibly have passed the ileocæcal junction in their final state. The history of the attack may commence in the first place with symptoms caused by the actual ulceration of the stone into the duodenum and the pain subsequently may travel round the abdomen with the stone. Rarely biliary calculi have been vomited when the fistula opened into the stomach, and instances have been described where the disappearance of a palpable gall-bladder has been followed by ileus. These patients are liable to report rather late to the surgeon, possibly because previous attacks have passed off and they have felt that the present one will do the same. The insidious danger of the vague intermittent nature of the symptoms cannot be overemphasized. On examination it may be possible to feel the stone either in the right iliac fossa or in a loop of the bowel in the pelvis where it may be detected on rectal or vaginal examination. Although the stones are not usually radio-opaque, the actual site of obstruction may be suggested by the X-ray findings provided that the obesity of the patient does not make it impossible to obtain a satisfactory picture. Gas and barium have been demonstrated in the biliary passages.

**The Formation of the Fistula.**—Stones which enter the intestinal tract via the common bile-duct are unlikely by reason of their size to produce intestinal obstruction except possibly by the acquisition of further layers in the course of months or years. Those stones which produce the typical biliary ileus enter the intestinal tract by a process of ulceration. Progressive fibrosis of the gall-bladder leads to pressure necrosis with inflammation and adhesion to an adjacent viscus and subsequent ulceration. The fistula communicates with the duodenum in about 85 per cent of cases; in the remainder, the stomach, ileum, and large bowel have all been involved. Experience shows that the fistula usually closes spontaneously. The other common causes of fistulæ between the biliary and intestinal tracts are peptic ulcer, new growth, and surgical trauma, but these constitute only 10 per cent of the total, the other 90 per cent being secondary to cholelithiasis.

**Complications.**—It is interesting to note that the complication of cholangitis is mentioned in only one of the articles which we have consulted, and in this one it is stated that cholangitis occurs in every case of bilio-intestinal fistula. Our view is that in cases arising primarily in the gall-bladder, the degree of fibrosis already present is such as to exclude the gastro-intestinal contents from the biliary tree, whereas should peptic ulcer, neoplasm, or external surgical trauma be the preceding factor, cholangitis may follow. A certain number of other complications have been described, though they are relatively uncommon. One instance has been found of ulceration of a stone into the duodenal bulb giving rise to the symptoms of pyloric stenosis. A barium meal showed a filling defect in the duodenum which was thought to be due to neoplasm, but at operation a large stone was found in the duodenal bulb and two more in the gall-bladder with the remains of a fistulous track. Volvulus of the loop containing the stone has been reported twice and a third case is recorded in this article. Recurrent obstructions are described, and also cases in which a stone has become impacted and later passed spontaneously per rectum only to be followed by a further obstruction due to a second stone. One case of impaction of a calculus in a rectosigmoid diverticulum has been reported. Perforation following impaction in the sigmoid colon has been described twice; one case was thought to be a carcinoma; both were treated by a Mikulicz type of operation. One case of colo-vaginal fistula was diagnosed at post-mortem.

**Treatment.**—Pre- and post-operative treatment will follow the accepted lines. The question of anæsthesia in this country is very straightforward. In one article local anæsthesia was suggested, but we felt that possibly this was due to the low standard of general anæsthesia in the country in question. When

the stone has been found, it should be moved back or moved on to avoid the congested area in which it has been impacted; this is followed by incision of the bowel in the longitudinal axis, removal of the stone, and transverse suture. Some authors have suggested crushing the stone either without opening the bowel (this has the obvious disadvantage of trauma to the bowel wall) or making a small hole and crushing the stone with a lithotrite, a procedure which must take longer than the simple extraction of the stone through a slightly larger opening. We consider the latter to be the better procedure. Further calculi should always be sought; the shape of the stone itself may suggest the existence of other stones. Closure of the fistula is not necessary as natural fibrosis will bring this about. In one of our cases, while searching for the cause of the trouble, the fistula was opened, but repair of the duodenum and drainage of the gall-bladder produced no ill effects.

## CASE REPORTS

*Case* 1.—Mrs. E. H., aged 58, was admitted to Frimley Hospital on July 20, 1950, with a diagnosis of doubtful intestinal obstruction. She was seen by Dr. F. Brockington and referred to one of us (P. J. M. W.) as a case of obstruction possibly due to gall-stones. On examination she was very shocked and collapsed. Diarrhœa and vomiting with intermittent colic were the main features: there was no definite past history. In spite of routine treatment she did not respond and at no stage was she fit for operation. She died on July 21.

Post-mortem examination was carried out (P. J. M. W.) and showed impaction of a large gall-stone 3 ft. from the ileocæcal junction; there were three congested patches in the proximal small intestine suggesting sites of temporary hold up of the stone, and a fistula was present between the gall-bladder and duodenum. This had already shrunk to about 1 cm. in diameter.

*Case* 2.—Mrs. E. C., a housewife, aged 68, was admitted as an emergency to Lincoln County Hospital on July 9, 1951. She gave a history of abdominal colic for thirty-six hours accompanied by repeated vomiting; the bowels had not been opened during the previous two days. At the time no history of previous attacks of abdominal pain was obtained, but subsequent inquiry from the patient's daughter revealed that many years previously ' gall-stones ' had been suspected.

The patient was an obese old lady seriously ill; she was dehydrated and her respiration was embarrassed. There were signs of peritonitis with generalized extreme abdominal tenderness maximal in the right iliac fossa. The tenderness and obesity combined to make impossible the palpation of any mass either abdominally or by rectal examination. Gastric suction and an intravenous glucose-saline drip were commenced and laparotomy was performed (P. A. T.) some forty-three hours after the onset of the abdominal pain. On opening the abdomen through a right paramedian incision free purulent fluid without smell was found in the peritoneal cavity. There was one matted loop of lower ileum covered with fibrinous exudate, which had undergone partial torsion. At the apex of the loop the lumen was obstructed by a single stone (*Fig.* 9). The appendix was not inflamed, but its mesentery was grossly œdematous. Dense adhesions around the gall-bladder were palpable, but no attempt was made to visualize this area.

The volvulus was untwisted and the stone removed through a longitudinal incision along the anti-mesenteric border of the bowel, immediately over the stone. The bowel wall appeared to be in spasm, thus preventing backward or forward manipulation of the stone. The incision in the ileum was closed by transverse suture in two layers. The calculus bore no facets and palpation of the ileum above the site of obstruction revealed no other stone. The abdomen was closed in layers without drainage.

Post-operative treatment was continued on the accepted principles of gastric aspiration through a Ryle's tube and the intravenous administration of saline and glucose-saline. A course of streptomycin was given for one week. The patient's progress was stormy; there was some degree of pulmonary collapse and signs of early

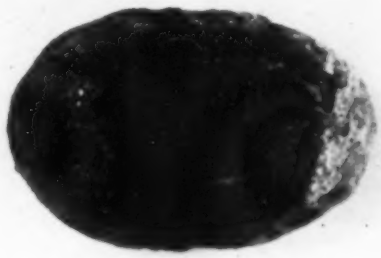

FIG. 9.—*Case* 2. The stone removed from a twisted loop of lower ileum.

cardiac failure developed. But the patient's will-power and the determined efforts of the nursing staff led to an unexpected recovery and she was transferred to convalescence a month after operation.

*Case* 3.—Mrs. R. T., a widow, aged 77, who lived alone. She was admitted to Louise Margaret Hospital on Sept. 15, 1951, with a tentative diagnosis of intestinal obstruction due to carcinoma of the colon. There was a history of persistent vomiting and colicky abdominal pain for one week; no bowel action had occurred during the previous two days. No history was obtained of previous attacks of abdominal pain.

This old lady of average build was dehydrated and seriously ill, but her mental condition was remarkably alert. The abdomen was distended and there was a large mass—rather smooth and mobile—in the left hypochondrium. Repeated small vomits occurred of fæculent fluid.

Gastric aspiration and an intravenous glucose saline drip were instituted; we were surprised when four pints of fluid were aspirated from the grossly dilated stomach, with a corresponding decrease in the abdominal distension. Laparotomy was performed (P. J. M. W.) under general anæsthesia (pentothal, cyclopropane, and tubarine). It was discovered that the tumour was a grossly enlarged spleen and that the intestinal obstruction was due to the impaction of a large gall-stone in the jejunum about 15 in. from the duodenojejunal flexure. There was no obvious cause for the splenomegaly. The obstructing stone was ' milked ' back up the jejunum for a few inches and then removed: its proximal end bore an obvious facet from contact with another stone, so a careful search was made. The fundus of the gall-bladder was adherent to the anterior surface of the first part of the duodenum and a second stone was felt to be actually passing through the fistula between the viscera; a third stone was palpable in the gall-bladder itself. The fistula was broken down by blunt dissection, the stones removed, the opening of the duodenum closed and the grossly fibrosed gall-bladder excised. The abdomen was closed, leaving a small drainage-tube down to the stump of the gall-bladder. The three calculi are shown in *Figs.* 10 and 11.

Post-operative treatment followed the usual routine of gastric aspiration with intravenous fluids, which in this case included one pint of blood. Streptomycin 0·5 g. was given eight-hourly for six days. Progress was satisfactory and five days after operation the gastric aspiration and intravenous drip were discontinued and the drainage-tube removed. Subsequently a wound infection with *B. coli* developed and a thrombosis in the left leg for which a course of tromexan was given. When a satisfactory conclusion to this case appeared likely a respiratory infection precipitated an attack of congestive cardiac failure and after a brief improvement the cardiac insufficiency became progressively worse until the patient died just three months after admission.

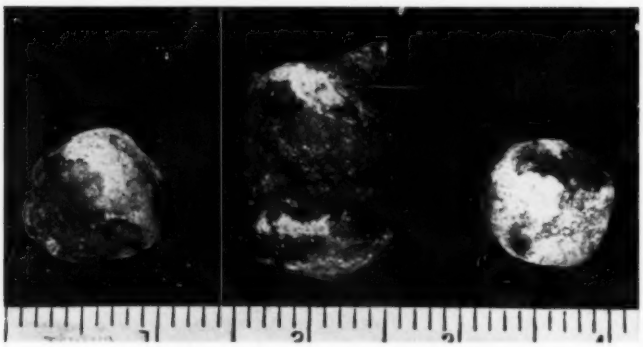

FIG. 10.—*Case* 3. The three stones removed. The large central stone caused the jejunal obstruction (*see* text): its upper end bears a single facet from contact with one of the other stones.

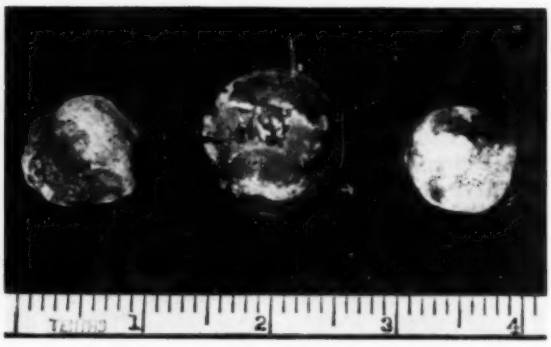

FIG. 11.—*Case* 3. Another view of the three stones showing the facet on one end of the obstructing stone.

## SUMMARY

Three cases of biliary ileus are reported; this is a rare cause of intestinal obstruction, but the syndrome follows a fairly clear-cut pattern, of which various features occurred in the cases described. We feel the correct pre-operative diagnosis is rarely made mainly because it is rarely thought of. We have endeavoured to present a summary of the literature to date.

For permission to publish *Case* 2 we are indebted to Mr. G. A. Bagot Walters, under whose care this patient was admitted. *Fig.* 9 is the work of the clinical photographer to Lincoln County Hospital and *Figs.* 10 and 11 were prepared by the Pathology Department of the Royal Army Medical College.

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# A NOTE ON THE TREATMENT OF CENTRAL DISLOCATION OF THE HIP-JOINT

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THIS note is intended to illustrate a method in the treatment of central dislocations of the hip-joint which has been used in the Traumatic Unit of the General Hospital, Birmingham, with, it is thought, some degree of success on 3 cases during the last few months. It is not presented with the idea of proving that the end-results in this injury are better by this method of treatment, but we have been so impressed by the early mobility obtained that we feel the method is worthy of further trial. An extensive search of the literature has been made and the only reference that we have been able to find is a short note by K. Lenggenhager (1946) in the *Schweizerische medizinische Wochenschrift*, although we had no prior cognizance of this article when the method was developed.

**The Idea.**—Mr. J. B. Leather, Senior Surgeon, suggested some time ago that if it were possible to put a direct pull on to the neck of the femur this would obviously have great mechanical advantages over the present method of indirect extension via the leg and the shaft of the femur; and hence a long screw, with ring attached, was introduced through the upper end of the shaft of the femur, immediately below and in the line of the neck. The types of screws are illustrated in the accompanying photograph (*Fig.* 12).

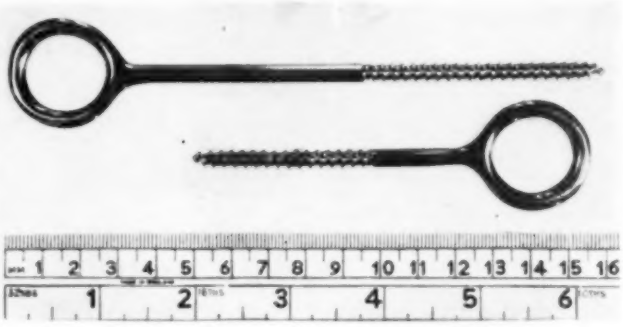
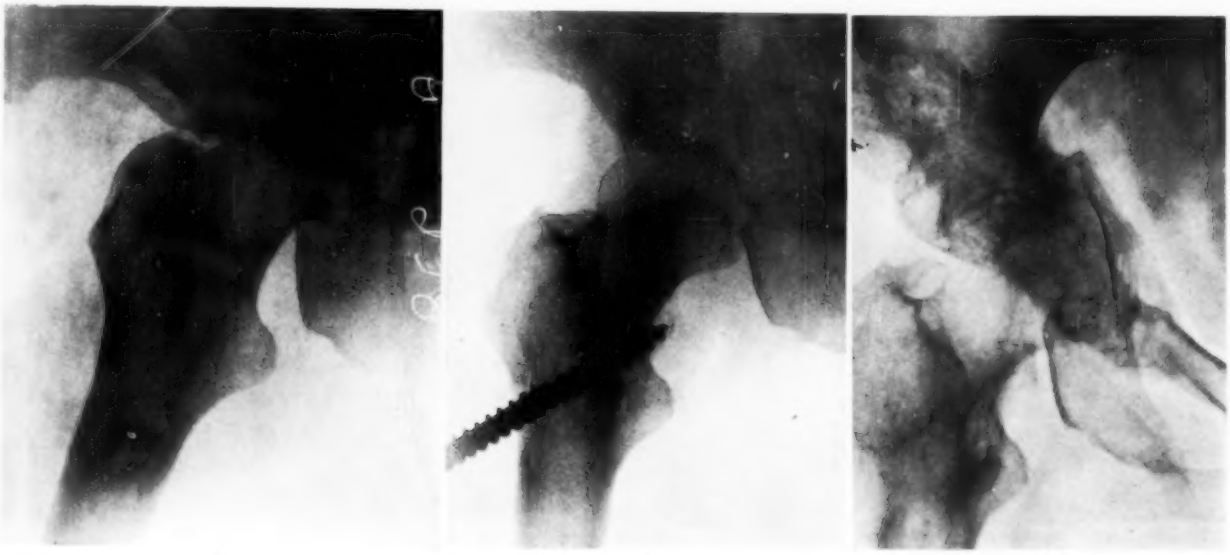


FIG. 12.—Types of screws used in treatment of central dislocation of the hip-joint.

**Method of Introduction of Screw.**—Under a general anæsthetic the affected leg is manipulated into a position of mild internal rotation and held in that position on a Hawley table. An incision is then made in the outer side of the thigh on to the great trochanter, which is cleared immediately below the gluteal ridge, and then, using X-ray control if necessary, a screw is inserted parallel with and immediately below the neck, if possible piercing both sides of the cortex. The wound is then closed in layers around the screw.

**Post-operative Treatment.**—The patient is returned to bed, the bed tilted 15° to one side, so that the affected side is uppermost, and a weight of 20 lb. is then attached to the ring of the screw and led over a pulley fixed to the side of the bed, thus exerting a very strong traction on the head of the femur in almost a direct line.

It was felt that this weight should be maintained for a period of not less than eight weeks. Unfortunately, and almost certainly due to the screw being of ordinary iron and not stainless steel, this ideal has



A B C

FIG. 13.—Mrs. N. A, Before traction; B, With screw and 20 lb. traction; C, Final result.

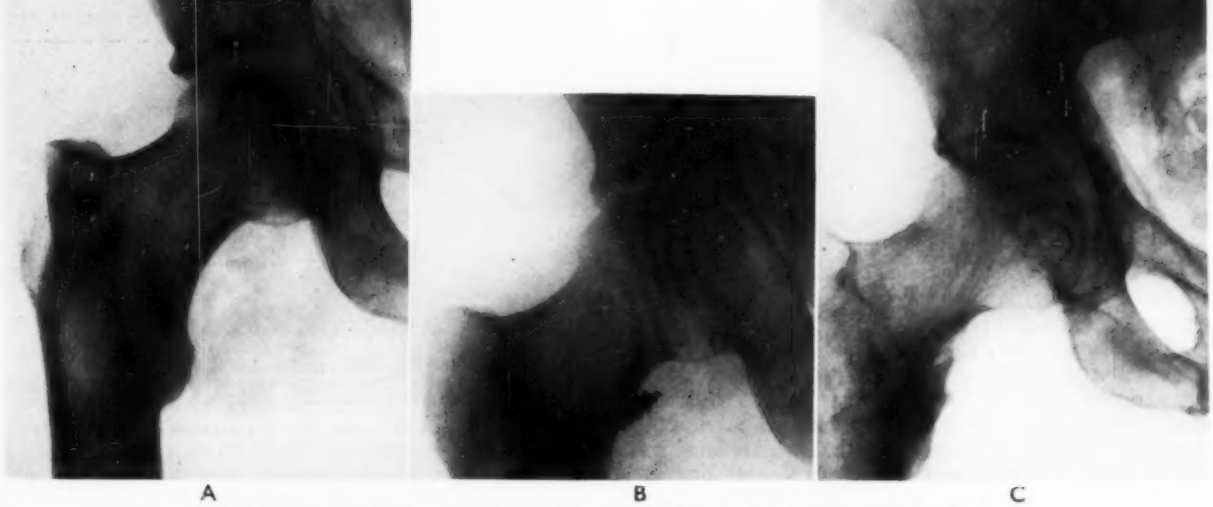
not been achieved and in two instances the screw pulled out at six weeks and seven weeks and in the third case, unfortunately, in four weeks. In no case has there been any marked infection around the track of the screw and all the wounds have healed very rapidly on removal of the screw.

During the time in which the pull is maintained active movements of the hip-joint are encouraged and it has indeed been remarkable to what extent movements have been possible, and it is felt that this is one of the advantages of this method, the suggestion being that the uniting surfaces of the acetabulum might be smoothed off by the continued action of the hip-joint.

The accompanying photographs illustrate the 3 cases before the insertion of this screw, and afterwards.

**Results.**—*Fig.* 13 shows those of the patient, Mrs. N., aged 66, who, as a result of a road traffic accident, sustained a traumatic amputation of the right leg below the knee and a central dislocation of the hip of the same side. The traction screw was inserted on Feb. 9, 1951, six days after the original injury, and pulled out spontaneously on March 23, 1951. Although the end-result here is not by any means good, it is suggested that without this screw the application of any traction would have been quite difficult.

*Fig.* 14 shows those of Mr. S. J., aged 59, who, as a result of a fall from a ladder on April 7, 1951, sustained a central dislocation of the right hip. On April 11 a screw was inserted, as described, and pulled out spontaneously on May 26. The latest radiograph of this man (Oct. 3, 1951) shows an



A B C

FIG. 14.—Mr. S. J. A, Before traction; B, With screw in situ; C, Final result.

A B C

FIG. 15.—Mrs. G. H. A, Before traction; B, With screw in situ (a rather lower insertion than we like); C, Final result, indicating than the head has sunk into the acetabulum.

extremely good result. He is walking without support and there is a full range of movement in this hip-joint.

*Fig.* 15 shows those of Mrs. G. H., aged 50, who, on April 30, 1951, sustained a central dislocation of the right hip. The screw was inserted under a general anæsthetic on May 1 and traction applied, but unfortunately the screw pulled out spontaneously on May 29 and *Fig.* 15 C illustrates the end-result despite the traction having been immediately replaced by a skin extension to the thigh and lower leg. It can be seen that there has been some re-displacement of the floor of the acetabulum.

## SUMMARY

A method is suggested of obtaining a better means of traction on the femur in the treatment of central dislocations of the hip-joint, although it is not suggested that the final end-results are any better.

Although we have had no personal experience of the methods, other ways have been used of pulling on the great trochanter, for example, by ice-tongue callipers and by a Kirschner wire through the trochanter, but these methods are all rather cumbersome and suffer from the disadvantage of restricting the movements of the hip-joint to some extent, and it is suggested that this simple screw is a better modification of this method.

Since the article was written, a fourth case has been treated in which traction was maintained for over eight weeks and again the immediate result was remarkably good.

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# VENTRICULOGRAPHIC CHANGES IN CYSTICERCOSIS OF THE BRAIN

By D. GOVINDA REDDY and B. RAMAMURTHY

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Reports on the frequent occurrence of cysticercosis of the brain in India are available from the published literature (Minchin, 1937; Menon and Veliath, 1940; McRobert, 1944; Gault and Balasubrahmanyan, 1948; Raman, Ramamurthi, and David, 1950; and Reddy, 1951). Most of the articles cover either the clinical manifestations or the autopsy findings with relevant histopathological changes, but information about ventriculographic findings is meagre. Any part of the brain may be infested with cysticerci, but the leptomeninges and the ventricles are more frequently involved. When the cysts occur in the cortical or subcortical regions they lead to the Jacksonian type of epilepsy. If they should project into the ventricle, one would expect to find changes in the ventriculographic features, as noticed in the following published case.

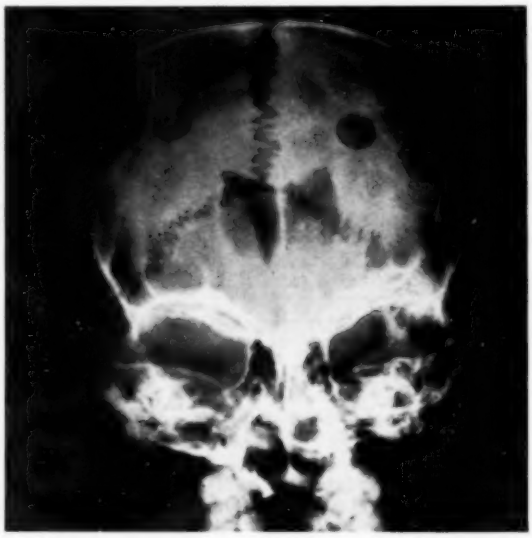

Fig. 16.—Ventriculogram—anteroposterior view. The body of the left lateral wall is irregular. The ventricles are not dilated and are normal in position.

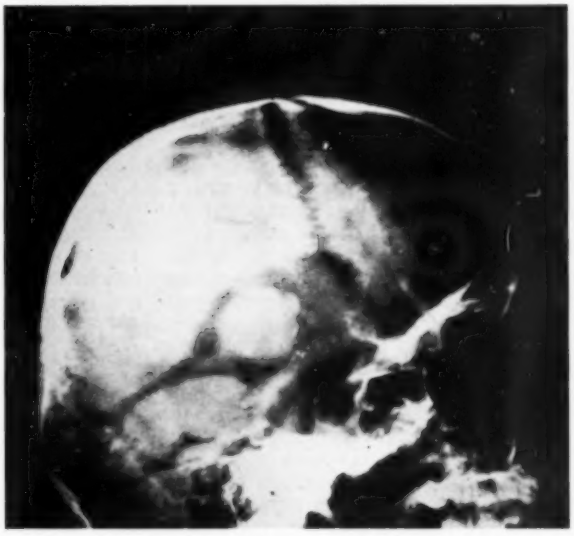

Fig. 17.—Ventriculogram—lateral view. Hemispherical protrusions are well seen in the superior and inferior surface of the body of the lateral ventricle.

## CASE REPORT

A Hindu girl, aged 12 years, was admitted into the wards of the Government General Hospital, Madras, with a history of headache for two years, occasional bouts of vomiting, and progressive dimness of vision. For the last three months she was having frequent fits, involving the right side of her body. After admission into the hospital the patient had several fits during which a detailed examination could be made. Before the patient went into a fit, she noticed a pulling sensation of the fingers on the right side, which gradually spread along the arm and later the entire body. After recovery from the fit, the right side of the body

continued to be weak, the leg recovering first and the hand last.

Physical examination revealed a well-nourished child. Fundus examination showed post-papillœdemic atrophy of both the optic disks. There was a concentric contraction of her fields of vision. No other neurological abnormalities were noticed.

As the child was having Jacksonian fits attended with increased intracranial pressure, a ventriculography was done to determine the nature and extent of the intracranial lesion. Bilateral posterior burr holes were made under local anæsthesia and the ventricles tapped, when an increased ventricular pressure was recorded on both sides, but there was no shifting of the ventricles. 12 c.c.

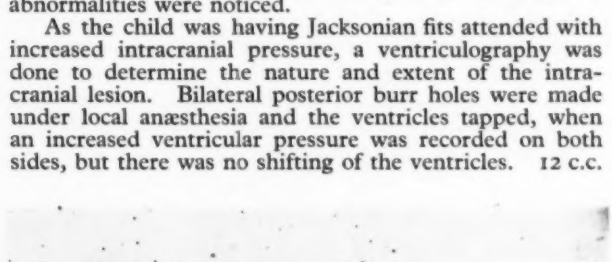

FIG. 18.—Section of *Cysticercus cellulosæ* removed from the cortex of the brain. (× 10.)

of air were put into each lateral ventricle and radiographs taken in various positions. The ventricles were normal in position, without evidence of dilatation. In the anteroposterior view (*Fig.* 16), some irregularity was noticed in the body of the left lateral ventricle. The lateral view (*Fig.* 17) showed more definite hemispherical filling defects in the wall of the ventricle. A diagnosis of multiple scattered lesions protruding into the ventricular system was made. Under endotracheal anæsthesia, a left lateral osteoplastic flap was turned. The dura was tense during tapping and the brain needle encountered areas of different consistency both hard and soft. On opening the dura, circular hard nodules were felt in the subcortical area in the post-central region. Most of the superficial ones were removed, leaving behind the deeper ones. As the intracranial pressure was high, it was decided to leave off, the bone and the operation was finished as a decompression. After the operation, the fits, headache, and vomiting were completely relieved and the vision showed signs of improvement. The follow-up of the case eight months after the operation shows freedom from fits, improved sight, and a residual weakness of the right hand.

PATHOLOGICAL REPORT.—The cysts varied in size from 3 mm. to 5 mm. They had white membranous walls. Histologically, one of the cysts examined showed a well-defined scolex lying free in the sac surrounded by fibrous tissue (*Fig.* 18). Outside this there was a layer of granulation tissue infiltrated with monocytes and occasional giant cells. Eosinophilic cells were not met with. The brain tissue outside the capsule was condensed, with glial proliferation.

## DISCUSSION

To diagnose infestation of the central nervous system by *Cysticercus cellulosæ*, one has to depend essentially on the clinical history of the patient. Dixon and Smithers (1934) have pointed out that in every case of epilepsy occurring in a patient with no family history of fits in childhood, the probability of cysticercosis must be entertained. The associated presence of cysticerci in the subcutaneous tissue and the somatic musculature strongly suggests or supports the suspicion of brain involvement. MacArthur (1934), Fairley (1934), and Dixon and Smithers (1934) have all found the intradermal and precipitin tests, using extract of *Cysticercus celullosæ* as antigen, not very satisfactory. The above tests are only group specific, very delicate, and liable to misinterpretation.

After calcification of the larvæ, roentgenograms of the skull may occasionally be helpful in locating the lesion. The possibility of diagnosing a case of cysticercosis of the brain by ventriculography, especially when they are located near the ventricles, has suggested itself to us from the observations made in the above case.

## SUMMARY

Ventriculographic changes in a case of cysticercosis of the brain are described. When the cysts protrude into the ventricles, the outlines of the ventricles show alterations which may help in confirming the diagnosis.

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# LIVER TUMOUR OF MIXED TYPE

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TUMOURS in early life are of special interest in oncology since the majority may be set apart from adult tumours because of their probable origin from embryonic cell-rests (Farber, 1947). They differ frequently from growths in adults in clinical and pathological characters. Early treatment is essential if treatment is to be successful. The following case concerns a rare but interesting tumour in the liver of a child.

## CASE REPORT

A thin, 2-year old boy was admitted to Paddington Green Hospital under the care of Dr. T. Pearse Williams on June 8, 1951, with obstructive jaundice which had been increasing in intensity for eight weeks. His skin and mucous membranes were a deep yellow colour and the lower border of the liver was palpable at the umbilicus. The spleen was not palpable. Laparotomy was carried out one week later by Mr. F. W. M. Pratt, when a smooth enlargement of the liver and gross distension of the gall-bladder were found. A cholecystgastrostomy was performed. From the pale bile aspirated from the gall-bladder, a pure culture of *B. coli* was grown.

On July 27 the patient was transferred to the care of Dr. R. Lightwood at St. Mary's Hospital, with signs of severe portal obstruction. A cystic area was felt above the umbilicus. During the following weeks the temperature was remittent (*Fig.* 19).

A second laparotomy was performed on Aug. 8, by Professor C. G. Rob, when a large cyst was found in the right lobe of the liver. The left lobe was solid. The

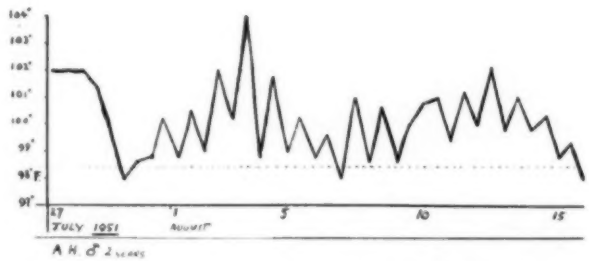


FIG. 19.—Remittent temperature registered in the patient. A typical example of 'biliary fever'.

cyst contained green mucus and a large amount of necrotic material. A biopsy specimen was taken from the cyst wall, upon which Professor W. D. Newcomb reported as follows: "The material consists of young, vascular fibrous tissue covered by a single layer of epithelium. In one fragment there are a few large irregular cells with much eosinophilic cytoplasm. The exact diagnosis is not obvious from this material, but intracanalicular adenofibroma might be suggested."

In the days following this second exploration the boy's condition quickly deteriorated. Through the laparotomy wound bile-stained fluid continued to be discharged for about three weeks. Blood-counts showed anæmia (hæmoglobin 10·4 g. per 100 ml.) with a high mean cell diameter of 8·5 μ indicating some hepatic failure. Terminally, a left pleural effusion developed. He died on Sept. 1.

POST-MORTEM EXAMINATION.—The body, which was 3 ft. (2·7 m.) in length, and 31 lb. (14 kg.) in weight, was examined thirty-six hours after death. The skin and mucous membranes were greenish-yellow in colour. A purpuric rash was present on the left side of the abdomen. The upper right paramedian abdominal scar contained a central ulcerated area about 3 cm. in diameter through which appeared a soft papillary mass. About 200 ml. of serous fluid were present in the peritoneal sac. The liver (2400 g.) contained a large cystic tumour projecting

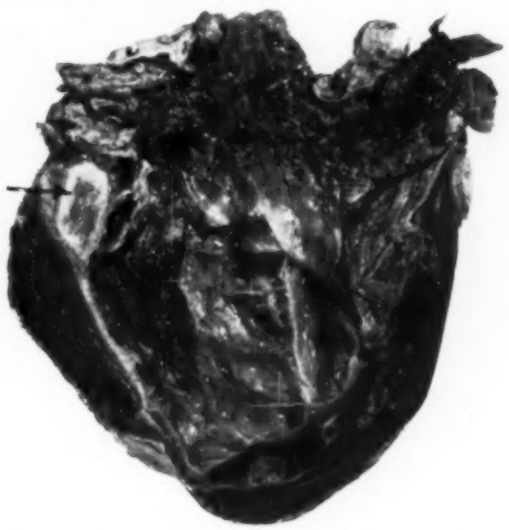

FIG. 20.—Sagittal section of liver showing the cystic nature of the tumour, which is surrounded by compressed liver tissue. The arrow indicates the paler, more solid portion in which striped muscle was present. (× ½.)

into the lumen of the right extrahepatic duct. The anastomosis between the fundus of the gall-bladder and the greater curvature of the stomach was healthy. About 200 ml. serous fluid were present in the left pleural sac. Both lower lobes of the lungs were collapsed and congested. The lymph-nodes of the ileocæcal, mesenteric, and paratracheal groups were enlarged. The femoral bone-marrow was dark green. The only important histological finding apart from those in the liver was the presence of many bile-pigment casts in the renal tubules.

*Description of Tumour.*—An area of about 6 cm. in diameter on the upper aspect of the right lobe of the liver was closely adherent to the anterior abdominal wall and was surrounded by a dense deposit of green fibrin. On section the liver was seen to consist mostly of a well-defined polycystic mass (*Fig.* 20). The cysts varied in diameter from 1 mm. to 3 cm. The largest cystic mass had a fibrous capsule and contained thin leaves of tissue separated by a glairy mucous substance. The surviving liver parenchyma was compressed and appeared as a greenish shell. A smooth polypoid portion of tumour, measuring 2 × 1 × 1 cm., protruded into the right extrahepatic duct, which was grossly distended. One part of the lower border of the tumour was conspicuously pale, solid, and ovoid, and measured 2 × 1·5 × 0·5 cm.

*Microscopically*, the cysts were lined by a layer of regularly arranged cubical or flattened epithelium (*Fig.* 21), reminiscent of bile-duct epithelium. Between the cysts there was an abundant connective tissue. This tissue contained scanty reticulin and collagen fibrils. Its cells were often scanty and round or oval in shape. Their nuclei frequently stained darkly with hæmatoxylin, though

many stained more delicately. In some places the connective-tissue cells were placed nearer to one another, the appearance then resembling embryonic mesenchymal tissue even more closely. The pale, solid area noted on macroscopical examination differed from the rest of the tissue in consisting of closely packed, round, polyhedral, spindle, or strap-like cells with large hyperchromatic nuclei (*Fig.* 22); most of these cells were lying haphazardly, but small numbers were arranged more

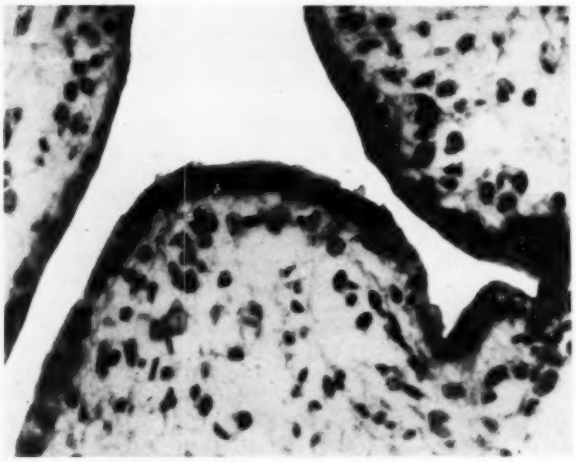

FIG. 21.—Portion of cyst wall. The lining of cubical cells is seen. Hæmatoxylin and eosin. (× 262·5.)

or less in parallel: these were more elongated and had a deeply eosinophilic cytoplasm in which transverse striations were sometimes clearly visible (*Fig.* 23). Sometimes two or three nuclei were present in these muscle cells. The surrounding liver parenchyma was

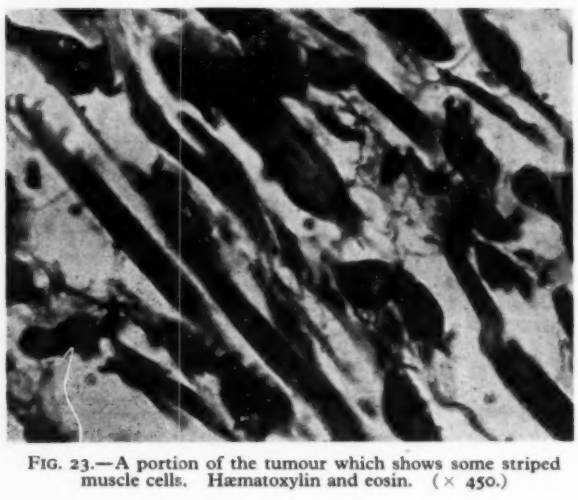

FIG. 23.—A portion of the tumour which shows some striped muscle cells. Hæmatoxylin and eosin. (× 450.)

compressed so that its cell columns were atrophic or else replaced by fibrous tissue (*Fig.* 24). Accumulations of bile-pigments were seen in some liver parenchymal cells.

No secondary deposits were found in lymph-nodes or elsewhere.

## DISCUSSION

Hepatomas, bile-duct carcinomas, and congenital cysts of the liver result from a perverted growth of epithelium. All are found mostly, though not exclusively, in adults. Liver carcinomata carry a poor prognosis, although for a long time the growth may be confined to the liver. Polycystic disease of the liver, on the other hand, is a relatively benign condition, compatible with long survival and often diagnosed only by accident (Comfort, Gray, Dahlin, and Whitesell, 1952). The so-called 'sarcomata' of liver are derived from disorderly mesenchymal or

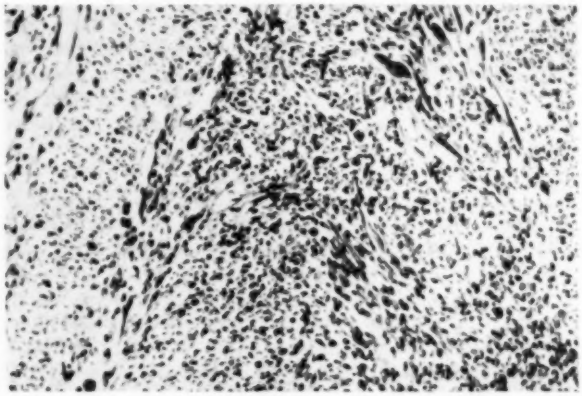

FIG. 22.—More cellular part of the tumour in which striped muscle cells are present. Hæmatoxylin and eosin. (× 64.)

mesoblastic growth. Their constituent cells have an embryonic appearance. Mixed tumours of the liver contain mixtures of epithelial and mesenchymal elements. Both the sarcomata and the mixed-liver tumours occur characteristically in early life. Like carcinomata, they carry a poor prognosis, but as a rule they metastasize only in the liver.

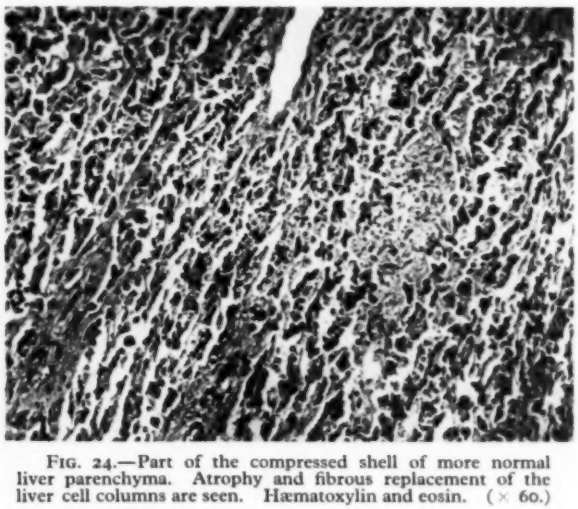

FIG. 24.—Part of the compressed shell of more normal liver parenchyma. Atrophy and fibrous replacement of the liver cell columns are seen. Hæmatoxylin and eosin. (× 60.)

McRae (1935) has stated that surgical removal should always be attempted, though this advice would seem to be a counsel of perfection.

The tumour described here was a mixed tumour consisting of multi-loculated, mucus-secreting cysts between which there was an embryonic type of connective tissue, part of which resembled an undifferentiated sarcoma and contained striped muscle cells. There was no evidence of carcinoma anywhere in the tumour.

This tumour had many features in common with a liver tumour described by Sheehan (1930) which was found in a 6-year-old girl and consisted of a number of cysts, lined by bile-duct epithelium, and embryonic cells. Some of the latter had differentiated into striated muscle. The hypoblast had not developed to carcinoma (hepatoma) but remained as the epithelium of benign cysts, while the embryonic connective-tissue cells underwent malignant development.

Besides the rare striated muscle, other types of heterotopic tissues may be found in embryonic tumours of the liver, e.g., cartilage (Hippel, 1910), osteoid (Webster, 1938; McRae, 1935), bone (Misick, 1898; Yamagiwa, 1911; Idzumi, 1913), bone and cartilage (Saltykow, 1914; Roth, 1938; Nissel, 1928), squamous epithelium (Roth, 1938; McRae, 1935).

The tumour here can be compared with Wilms' tumour of the kidney. The patient had no abnormality of his kidneys.

## SUMMARY

A liver tumour in a 2-year-old male is described. It consisted mostly of multilocular benign cysts presumed to be of bile-duct type, but it also contained malignant mesenchymal tissue, including rhabdomyomatous cells. There were no metastases. The tumour is in some respects comparable with Wilms' tumour of the kidney.

I am indebted to Dr. Ernst Neumark, who performed the necropsy and who helped with the preparation of the script; to Professor W. D. Newcomb for advice; to the clinicians concerned for permission to publish details of the case; and, finally, to Mr. Alec Beasley and the Photographic Unit of St. Mary's Hospital for technical assistance.

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# CONGENITAL ARCHENTERIC CYSTS

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EPITHELIAL-LINED cysts are found in relation to any part of the gastro-intestinal tract (Ladd and Gross, 1940; Ladd and Scott, 1944). They may be structurally independent of the gut, or the muscular layer may be common to cyst and gut, with a dividing partition of mucous membrane. The epithelial lining of these cysts does not necessarily correspond to that of the adjacent gut. Thoracic cysts may be lined with typical œsophageal, bronchial, or gastric mucous membrane, and the various types of mucous membrane may be found in different parts of any one thoracic cyst. There is no recorded case with a primary communication between the cyst and the gastro-intestinal tract (Nicholls, 1940; Ladd and Scott, 1944; Davis and Salkin, 1947). Pathologically, clinically, and probably also developmentally, they differ from duplications of the gut, such as double-barrelled colon, partial doubling of the œsophagus, etc., (where there is primary communication between the duplication and the gut proper). Williams and Johnson (1952) found records in the literature of 32 cases of intrathoracic 'gastric cysts'. In comparison, there are few references in the literature to doubling of the œsophagus. Frank and Paul (1949), describing 1 case, found only 2 others in the literature, and Professor Johnstone, of Leeds, has given details of 2 similar cases (personal communication). A variety of names have been applied to these cysts, all of them inappropriate. Either they are not sufficiently comprehensive and indicate only one particular type of cyst—for example, 'gastrogenic', 'bronchogenic', 'enterogenous' cysts—or they are misleading both as regards their anatomy and aetiology, for example 'diverticulum' or 'duplication'. The title of this article—Congenital Archenteric Cysts—surmounts those objections and is sufficiently comprehensive to include all the types of congenital cysts related to the alimentary canal, while indicating their origin from the primitive gut.

The following is an account of a case of congenital archenteric cyst with unusual features, together with a discussion of the embryological significance and possible aetiology of the condition.

## CASE REPORT

HISTORY.—The patient, M. M., was born in 1933, an apparently healthy and normal baby, the elder child of a family of two. At 18 months she began to experience spasmodic attacks of pain in the lower chest and upper abdomen, accompanied by a harsh cough. The initial pain occurred when solids were first added to the feeds, but the onset of subsequent attacks was quite unpredictable. As little as half an hour or as long as several days intervened between the bouts, which lasted 5–7 minutes. They occurred at any time of the day or night and bore no relation to time of feeding.

When 4 years old, the patient developed 'pneumonia' and was later admitted to Mearnskirk Hospital, Glasgow, under the care of Dr. A. Dale. Radiological examination revealed no evidence of pulmonary tuberculosis but a large shadow was seen to the right of the vertebral column and running parallel to it. Following a barium swallow, the opaque medium passed freely through an opening on the right side of the œsophagus about the level of the

seventh dorsal vertebra and outlined a pocket extending roughly from the level of the first to the tenth dorsal vertebra. Œsophagoscopy was performed by Dr. A. Brown Kelly at the Royal Hospital for Sick Children, Glasgow. The upper part of the gullet was normal, but at 17 cm. from the incisor teeth there was evidence of the presence of two channels, both of which could be examined with ease. A diagnosis of œsophago-mediastinal fistula was made. The case was recorded in the *Journal of Laryngology and Otology* (Kelly and Henderson, 1939).

Throughout this period of investigation the symptoms continued, but the attacks became less frequent and less severe. It was found that relief could be obtained by alterations in posture, and for the next few years it was the parents' custom to ' empty the cyst ' by inverting the child at regular intervals and slapping her on the back.

FIG. 25.—The cyst partly filled and otherwise outlined by barium.

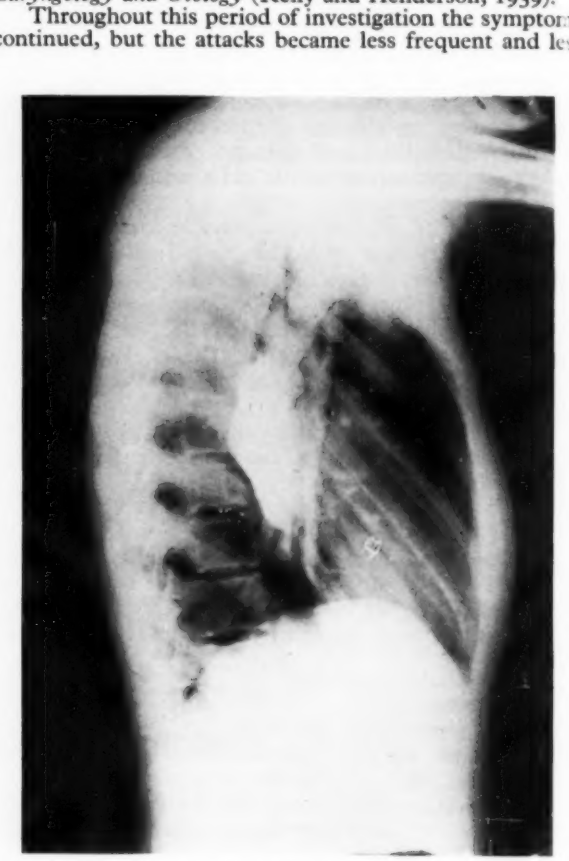

FIG. 26.—Barium is passing down the normal œsophagus and also through the fistula to fill the cyst.

FIG. 27.—Congenital fusion of cervical vertebræ.

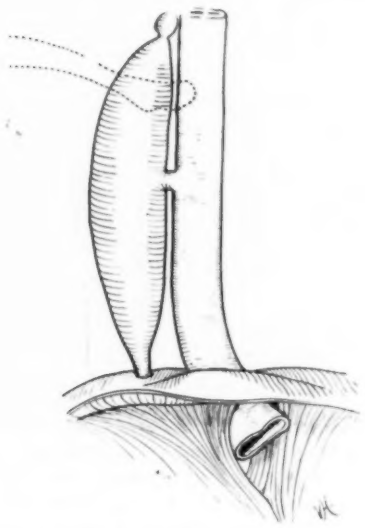

FIG. 28.—Line drawing showing the cyst, œsophagus, and fistulous communication.

This manœuvre was so successful in aborting spasms of pain that it was adopted as a routine ' prophylactic ' measure after meals. By the age of ten, the pains had disappeared and she enjoyed good health until her eighteenth birthday when she complained of a constant dull aching pain in the back. Anorexia and lassitude developed and, for the first time, vomiting became a feature. There was never any difficulty in swallowing, but the patient's general condition deteriorated so much that she became confined to bed.

On admission to Glasgow Royal Infirmary (Sept. 26, 1951) the patient was nervous and apprehensive and complained of pain in the back and the epigastrium. There was persistent vomiting and even the swallowing of water was difficult and painful.

Examination revealed marked emaciation and dehydration (weight 71 lb.) in a girl of poor physique. The neck was short and there was a slight cervical scoliosis.

Following barium X-ray examination, Dr. Raeside reported as follows : " Barium swallow shows an extensive tubular ' diverticulum ' extending from 2 in. above the clavicle down to the level of the tenth dorsal vertebra (*Fig.* 25). The only opening defined into the diverticulum is at the middle third of the œsophagus (*Fig.* 26). The position of this abnormal tube is to the right of the midline posterolateral to the œsophagus. There is a congenital abnormality of the cervicodorsal region, with vertebral fusion and kyphosis (*Fig.* 27). Sacral spina bifida is also present."

*Œsophagoscopy* (Oct. 5) : The lower two-thirds of the œsophagus was acutely inflamed. While no abnormal

FIG. 29.—Cervical fistula lined with gastric mucous membrane, discharging acid secretion and causing excoriation and ulceration of the skin.

orifice was seen, barium and frothy mucus kept filling the œsophagus as the instrument was withdrawn, and this fluid appeared to be entering the lumen about 19 cm. from the incisor teeth, indicating a communication between the abnormal tube and normal œsophagus.

TREATMENT.—The only adequate treatment appeared to be excision of the ' diverticulum ' but, in view of the patient's poor general condition and the probable difficulty in feeding her in the immediate post-operative period, a gastrostomy was performed on Oct. 10.

AT OPERATION (Nov. 2).—Anæsthetic (Dr. Douglas McAlpine) : Intravenous thiopentone, followed by gas and oxygen, tubarine, and cyclopropane.

Right-sided thoracotomy was performed through the bed of the seventh rib. A tubular swelling occupied the posterior mediastinum from the upper limit of the thorax to the diaphragm (*Fig.* 28). The appearance was that of a dilated tube, constricted at the crossing of the azygos vein. An œsophageal tube passed down the normal œsophagus, could be palpated through the walls of the swelling, and the site of the fistula was a thickened and fibrosed area situated at the level of the seventh dorsal vertebra. The mediastinal pleura and the azygos vein were divided and it was now seen that the tubular swelling extended below the fistula to the diaphragm, and above

FIG. 30.—Post-operative radiograph showing the normal œsophagus.

into the root of the neck. The part below the fistula was dissected free. The lower end, which tapered to a solid cord of epithelial tissue, was enveloped by the muscle-fibres of the diaphragm as in the normal œsophagus. The upper limb, which was closely related to the trachea, extended well above the clavicle so that removal became both difficult and dangerous, and it was decided not to attempt any further dissection from below. The region of the fistula was then explored. It was divided and the opening in the œsophagus was closed with a layer of interrupted catgut sutures and a second layer of interrupted silk sutures. The tube was ligated and divided as high up as possible, the bulk of it being removed from the thorax and the upper remnant pushed up into the neck. An oblique incision was made in the lower part of the right side of the neck to reach the superior mediastinum, from which the upper pocket of the cyst was delivered and exteriorized as a cervical fistula.

*Post-operative course* : Fluids by mouth were given on the fourth post-operative day, and at the end of four weeks full diet was taken by mouth, the gastrostomy tube was removed, and the gastrostomy wound closed spontaneously.

The skin around the fistula in the neck became increasingly excoriated and deeply ulcerated, causing much pain (*Fig.* 29). On Dec. 19 the cervical portion

of the cyst was excised. The highest part of the sac consisted of a small recess lined by pale smooth mucous membrane and firmly adherent to the cervical vertebræ. It was impossible to excise this portion, and its mucous membrane was destroyed by coagulating diathermy current. Post-operative X-ray examination (*Fig.* 30) showed that barium passes freely down the normal œsophagus.

DESCRIPTION OF SPECIMEN.—The reconstructed specimen consists of a tube closed at both ends, with a pyloric glands towards the lower end. Typical Brunner's glands can be seen in the submucosa of the intestinal areas. The muscularis mucosæ consists of two layers, in parts hypertrophied. The submucosa is broad and loose, with numerous large blood-vessels and, at the lower end of the specimen in the 'intestinal' area, contains glandular tissue of the mixed salivary type, with well-defined crescents (*Fig.* 33). Obviously, this glandular tissue has an endodermal origin like that which is sometimes present in the trachea, although salivary tissue is generally

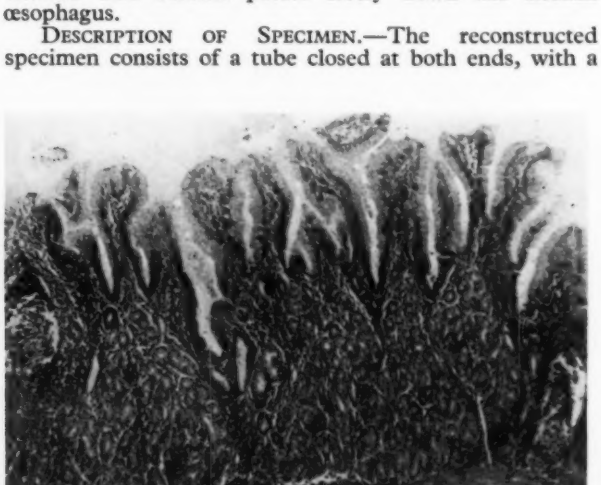

FIG. 31.—Gastric mucous membrane.

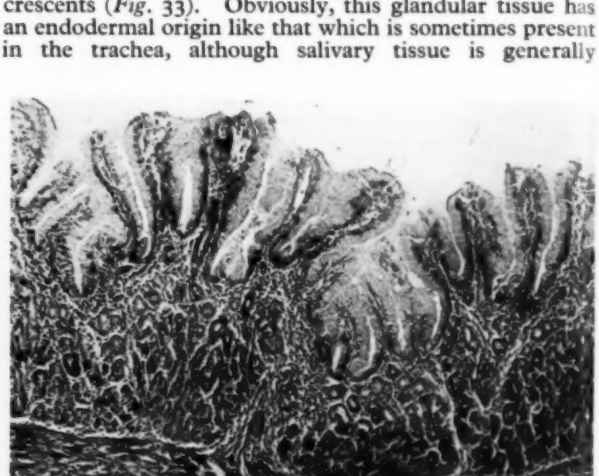

FIG. 32.—Intestinal-type mucous membrane.

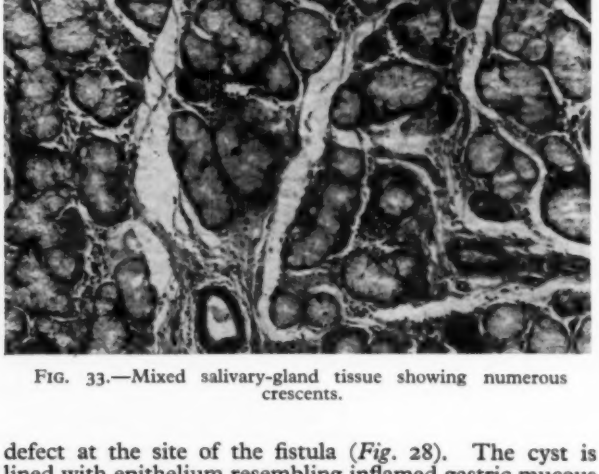

FIG. 33.—Mixed salivary-gland tissue showing numerous crescents.

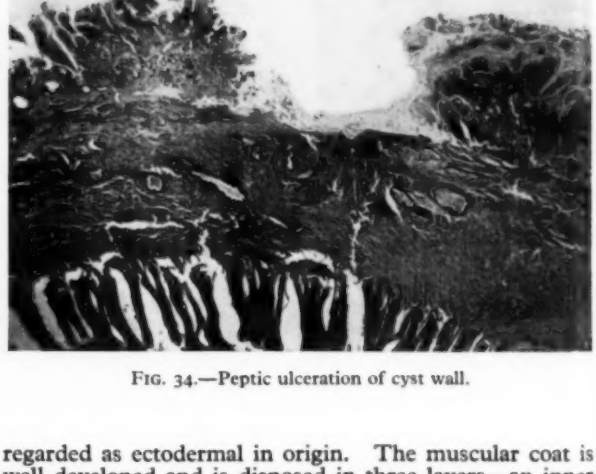

FIG. 34.—Peptic ulceration of cyst wall.

defect at the site of the fistula (*Fig.* 28). The cyst is lined with epithelium resembling inflamed gastric mucous membrane, except at its upper end where it is lined with pale smooth epithelium. The cyst wall is about the same thickness as the normal œsophagus, with well-developed muscular layers. At the site of the fistula there is evidence of thickening and fibrosis similar to the edge of a chronic peptic ulcer.

*Histology.*—The specimen is lined with gastric mucous membrane (*Fig.* 31). There are tall columnar epithelial cells with no cuticle and chief and oxyntic cells are present. Towards the lower end of the specimen there are areas of intestinal mucous membrane (*Fig.* 32), although there are no villi. These areas are identified by the presence of scattered goblet cells and by the clearly demarcated cell edges with well-defined cuticle. The tunica propria shows an intense lymphocytic infiltration with, in addition, numerous solitary follicles. The lymph-follicles are larger in the 'intestinal' areas. In the gastric area there are mainly fundus-type glands, with clusters of regarded as ectodermal in origin. The muscular coat is well developed and is disposed in three layers—an inner longitudinal layer, an intermediate circular layer, and an outer longitudinal layer. This last layer is deficient in some areas. Occasionally in the outer layer there are skeletal or striated muscle-fibres. Between the inner and the middle muscle coats there is a rich myenteric plexus which is more abundant than that found in the œsophagus. Throughout the mucosa there are many areas of ulceration resembling small peptic ulcers (*Fig.* 34).

## DISCUSSION

Intrathoracic cysts lined by epithelium of endodermal origin and related to the œsophagus are relatively uncommon.

The great majority of these cysts are encountered in young children and demand treatment before 3 years of age. Ladd and Scott (1944) stated that the oldest recorded case occurred at 3½ years, while

Williams and Johnson (1952) found that 70 per cent of 32 cases studied were under 2 years and 90 per cent were under 6 years. Without operation, the closed cyst may enlarge and cause respiratory or cardiac embarrassment, or there may be ulceration followed by rupture into the mediastinum or pleural cavity.

The history of the above case is interpreted in this way: the presenting symptoms of pain and cough at 18 months are typical of an enlarging mediastinal cyst. At 4 years there was an acute illness which, it is suggested, was due to the rupture of the cyst into the normal œsophagus. For fourteen years she remained fairly well because the cyst could be emptied through the fistula, particularly if encouraged by postural treatment. The recurrence of symptoms at 18 years is considered to have been due to inflammation and ulceration within the cyst and secondary acute œsophagitis.

The cyst described here differs essentially from the condition of acquired diverticulum of the œsophagus. Although small traction diverticuli are found at the mid-œsophageal level, the large diverticuli are usually found at the lower end. The tubular shape of the cyst extending from the neck to the diaphragm is quite different from the characteristically rounded pulsion diverticulum. With the exception of patches of intestinal mucous membrane below, the epithelial lining of the cyst is mainly gastric mucous membrane and, moreover, the cyst possesses in its own right all the structural components of normal gut. Microscopical examination of the specimen supports the view that the fistula resulted from peptic ulceration and perforation, and this was still further confirmed by the presence of numerous small peptic ulcers elsewhere in the cyst. An alternative diagnosis of duplication of the œsophagus was ruled out by the gross anatomical features of the condition. In true œsophageal duplications there are communications with the normal gullet above and below.

The case-history, the gross anatomy, and the histology of this anomaly all indicate that the condition was primarily a congenital archenteric cyst, with secondary ulceration and fistulous communication with a normal œsophagus. It is generally agreed that these cysts are congenital and not acquired, and some clue to their origin may be given by the embryology of the gut.

The endodermal tube which represents the primitive gut is the part of the yolk sac or archenteron, taken into the body of the embryo about the end of the third week, when the hitherto flat trilaminar disk develops transverse and craniocaudal convexities. With the further folding at the head and tail ends of the embryo, the enclosed portion of the yolk-sac can be divided into foregut, midgut, and hindgut. The primitive foregut, the anlagen of the œsophagus and stomach, is at first limited to the dorso-pericardial region cranial to the early septum transversum. It lengthens *pari passu* with the growth and expansion of the branchial arch system, which separates pericardium and stomatodæum and is responsible for the final emergence of a 'neck' and gullet. In the 5-mm. embryo (35 days) the œsophagus is 1 mm. long, but it increases rapidly thereafter, especially the lower end, which is related to the ventral aspect of the septum transversum. At an early stage there is proliferation of the cells of the endodermal tube, forming a multi-layered, thick epithelial lining which, for a period, almost obliterates the lumen. The non-epithelial elements of the œsophageal wall are secondary contributions from the lateral mesoderm, which, in this region, does not split to form a cœlom. At 5 mm. the epithelial tube becomes surrounded by a mass of mesenchyme which differentiates into first a circular and later a longitudinal layer of muscle. About the end of the sixth week (14-mm.), a process of vacuolation commences which gradually reconstitutes a lumen (Johnson, 1910). This vacuolation only affects the inner layer of the epithelium and therefore cannot be the mechanism responsible for a duplication as has been suggested (Keith, 1933). In embryos of about 4 mm. there is a median outgrowth from the lower pharynx which divides to form the early lung buds. Histogenic differentiation of gut epithelium commences about the 15-mm. stage and is well advanced by 17-mm.* The specific differences in the structure of the alimentary mucous membrane are determined on a regional basis according to a recognized pattern. The nature of the inductive influence is, however, unknown.

The condition of congenital archenteric cyst has been variously explained as (*a*) an embryonic diverticulum, when it would be expected that it would retain a communication with the parent tube—this is not so; (*b*) an anomaly related to the pulmonary outgrowth—an explanation which neglects the potential ubiquity of these cysts. Suggestions that the cysts are remnants of the vitelline duct or result from the vacuolation process are merely irrelevant. Having regard to the post-natal structure and known embryology, the following is offered as a rational interpretation of the condition. At an early stage, probably in presomite embryos at the time of the commencing involution of the trilaminar disk, a segment of endoderm becomes segregated and in some way gets out of place and fails to become incorporated as part of the substance of the embryonic gut. It has, however, been determined and retains its endodermal competence. It thus responds to the appropriate inductive stimuli and develops, although isolated from the rest of the gut. Being out of position and to that extent disorientated, its histogenic differentiation is less specific and precise. Thus the mucous membrane of these cysts may display a variegated pattern, reflecting all the developmental potential of endodermal tissue. On these grounds it is therefore submitted that the term 'congenital archenteric cyst' is sufficiently comprehensive to include the diversity in structure and position of these cysts, and does not offend their essential aetiology.

## SUMMARY

A congenital epithelial-lined cyst of the mediastinum having a fistulous communication with the œsophagus is recorded.

The surgical treatment and histological structure are described.

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* *Contributions to Embryology*, 1942, **30**, 232. Carnegie Institute, Washington.

The embryological significance and possible aetiology are discussed.

The term ' archenteric cyst ' is submitted as the most appropriate name for this condition.

We wish to express our thanks to Mr. G. H. Stevenson for his advice and encouragement and for permission to publish this case.

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# ARGENTAFFIN CARCINOMATA

## WITH SPECIAL REFERENCE TO GROWTHS OF THE ILEOCÆCAL VALVE

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DURING the last thirty years of the nineteenth century a number of small submucous tumours of the ileum and jejunum were recorded, mostly by German authors. The tumours were incidental autopsy findings and were yellow or white in colour. Because they had the histological structure of an undifferentiated carcinoma but appeared to be slow-growing and non-invasive, Oberndorfer (1907) called them carcinoid tumours. During succeeding years it was recognized that they were commoner in the appendix than in the small intestine, but their origin remained in doubt until Gosset and Masson (1914) proved they arose from the cells of the gastro-intestinal mucous membrane described by Kultschitzky in 1897. These cells were in fact originally described in 1870 by Heidenhain, who also demonstrated their affinity for chromium salts. Gosset and Masson showed that both the ' Kultschitzky ' cells and the cells of the carcinoid tumour had the power of reducing ammoniacal silver salts to metallic silver. Unlike the chromaffin reaction, this property is not shared by any other type of cell to a comparable degree.

In recent years a very large number of papers has been written about these tumours. It is now known that they may occur anywhere in the gastro-intestinal tract from the cardiac orifice of the stomach to the anorectal junction, although the majority are found in the appendix and the lower part of the ileum. The original conception of their innocent nature has had to be abandoned, as metastases have occurred in many of the recorded cases. In spite of its power of invasion and tendency to metastasize, however, the argentaffin carcinoma grows extremely slowly and several cases are on record in which patients harbouring inoperable metastases have remained in good health for many years. Such a case is described by Porter and Whelan (1939), the patient being well ten years after the removal of a tumour of the small intestine, although a mass of invaded lymph-nodes had been left in situ.

Despite the large number of cases recorded, a correct clinical diagnosis has been an extremely rare event, except when the tumour occurred in the rectum and was accessible to biopsy. In this paper it is hoped to show that argentaffin carcinomata of the ileocæcal valve may give a sufficiently characteristic clinical picture to justify a pre-operative diagnosis. The tumour also appears to metastasize more often from this site than from any other.

## MALIGNANCY AND CLINICAL FEATURES OF ARGENTAFFIN CARCINOMATA

**Appendix.**—This is the commonest site at which argentaffin carcinomata occur, the reported incidence varying from 0·1 per cent to 0·5 per cent of surgically removed appendices. (Moore, 1938 ; Hopping, Dockerty, and Masson, 1942). Up to the present time, however, only 18 cases have been recorded in which the tumour had spread beyond the wall of the appendix, and in only 11 of these had actual metastasis occurred. (Moore, 1938 ; Latimer, 1941 ; Hopping, Dockerty, and Masson, 1942 ; Reid, 1948.)

Apart from the rare metastasizing cases the majority of argentaffin carcinomata of the appendix are incidental findings in operative specimens. Three-quarters of the tumours are situated in the distal one-third of the appendix and the average age at which they occur is 25 years. Their relation to acute and chronic appendicular disease is difficult to determine. In the acutely inflamed appendix the growth may lie at the point of obstruction, but more often it is situated nearer the tip. In appendices with chronic inflammatory changes, Masson (1928) has shown that microscopical neuromata may arise in the nerve-plexus of the mucous membrane and that argentaffin cells proliferate within their constituent fibres. Escape of argentaffin cells into the connective tissue and lymphatic spaces may give rise to an argentaffin tumour.

**Small Intestine.—**

*Jejunum and Ileum.*—Up to 1948 over 300 argentaffin carcinomata of the jejunum and ileum had been reported (Reid, 1948). Multiple growths are present in from 20 to 50 per cent of cases according to various estimates, and one case has been described in which sixty-eight separate tumours were present (Dockerty and Ashburn, 1943). The

mesentery is frequently invaded, and Ariel (1939) found that metastases had occurred in 25 per cent of cases. The regional lymph-nodes are affected most frequently and the liver less often, while widespread metastases occur occasionally.

Clinical manifestations have occurred in 25 per cent of recorded cases also (Ariel, 1939). The remainder are mostly small growths confined to the submucosa and found incidentally at autopsy. The symptoms are usually the result of partial intestinal obstruction and consist of episodes of colicky abdominal pain and vomiting, often associated with diarrhœa. In 13 cases described by Dockerty and Ashburn (1943) the average duration of symptoms was three and a half years.

Obstruction is usually caused by kinking of the bowel, the result of fibrosis which occurs when the growth penetrates the muscular coats and proliferates in the subserous layer. Occasionally it is due to annular constriction, intussusception, or adhesion of neighbouring loops to the tumour. Ulceration occurs frequently, but is rarely more than superficial, explaining the fact that only traces of occult blood can be found in the stools (Dockerty and Ashburn, 1943).

With regard to radiological diagnosis, Miller and Herrmann (1942) have demonstrated a small filling defect and kinking of the bowel at the site of partial obstruction in 2 cases. They believe this appearance is highly suggestive of an argentaffin carcinoma and were able to make a correct pre-operative diagnosis in one of their cases.

*Duodenum.*—Fourteen argentaffin carcinomata of the duodenum have been traced, only 1 of which metastasized (Saltykow, 1912; Raiford, 1933; Feyrter, 1934; Polivy, 1950; Hannan, Hazard, and Wise, 1951). All except two were less than 2 cm. in diameter, and there were four separate tumours in 2 cases. Eight were incidental autopsy findings, 3 were found during investigation of other upper abdominal conditions, and 3 were the cause of symptoms.

Of the last group, two were small tumours of the first part of the duodenum and caused epigastric pain and vomiting. The other measured 6 × 5 cm. and involved the duodenal papilla, causing steatorrhœa and loss of weight.

Five of the 6 cases found during life were demonstrated radiologically as filling defects. Adenocarcinoma was suspected in the case with steatorrhœa, but the remainder, all of which were in the first part of the duodenum, were diagnosed as benign polyps. All were successfully removed by local excision, except one which was situated in the portion of duodenum resected during a subtotal gastrectomy.

**Large Intestine.**—

*Cæcum.*—Twenty-one cases involving the cæcum have been described, 11 of which have metastasized (Aalkjær, 1937; Waugh and Snyder, 1941; Satory, 1942; Altman and Mann, 1948; Brown, Bissonnette, and Steele, 1949; Cruickshank and Cunningham, 1949; Pearson and Fitzgerald, 1949; Horn, 1949). The growths varied in character from one or more nodules 0·5 cm. or less in diameter to an ulcerated mass measuring 11 cm. In 8 cases, including some of the larger growths, there were no gastro-intestinal symptoms, the tumours being discovered unexpectedly at operation or autopsy. Discussing cases in which symptoms were present, Horn (1949) states that the clinical, radiological, and sometimes even the gross pathological features are those of adenocarcinoma.

*Colon.*—Seven argentaffin carcinomata of the colon are recorded (Reid, 1948; Horn, 1949), 2 in each of the ascending, transverse, and sigmoid portions, and 1 in the descending colon. Three of the tumours metastasized. Clinical data are available in 6 cases, all of which had gastro-intestinal symptoms and were diagnosed as adenocarcinomata.

*Rectum.*—This type of tumour has been described in the rectum on eighty occasions (Raven, 1950; Rosser, 1951; Tavenner, Bacon, and Peale, 1951). It is usually symptomless and is found on routine examination of the rectum as a submucous nodule or a small polyp. Occasionally it infiltrates the muscular wall of the rectum, ulcerates or assumes an annular form, giving rise to symptoms indistinguishable from those of carcinoma. The diagnosis can be made histologically after local excision or biopsy.

Metastases have occurred in only 9 cases. In contrast with the slow progress of most metastasizing argentaffin carcinomata, widespread dissemination occurred rapidly in 7 cases and caused early death, the primary growth in 2 of these cases remaining a small submucous nodule.

These rectal growths also differ from argentaffin carcinomata elsewhere in their histological features. While the typical cords of round or polygonal cells can usually be recognized, the bulk of the tumour is commonly formed by ribbon-like festoons of columnar and prismatic cells. Occasional argentaffin granules have been demonstrated in some of the cases, but they are entirely absent from the majority. Stout (1942) suggests that this is because the rectal growths are formed from homologues of the argentaffin cells in an earlier phase of differentiation and before they have acquired argentaffin properties.

**Stomach.**—Of 24 cases recorded up to the present, 5 have metastasized (Reid, 1948; Pearson and Fitzgerald, 1949; Cruickshank and Cunningham, 1949; Jonsson, 1949; Marshak and Friedman, 1951). Fifteen cases are discussed by Wirts and Breckenridge (1949), of which 9 were found incidentally at autopsy and 6 caused gastric symptoms. The symptoms were in no way characteristic and included epigastric pain, anorexia, vomiting, hæmatemesis, melæna, and loss of weight. Radiography suggested polyposis in 1 case in which six separate tumours were present, while in the authors' case a benign tumour was diagnosed though in fact metastases to the regional nodes had occurred.

## CASE REPORT

HISTORY.—G. A., a 57-year old man, was admitted to hospital on Feb. 20, 1950. For the previous four years he had suffered from attacks of lower abdominal pain and vomiting at intervals of approximately three months. Between the attacks he had been perfectly well. Latterly the attacks had become more frequent and he had become increasingly constipated. No blood had been passed per rectum and he had lost 1 st. in weight.

ON EXAMINATION.—A thin, slightly built man. The abdomen was a little distended and peristalsis could be seen. A firm mass about 2 in. (5 cm.) in diameter was

felt in the right iliac fossa. It was almost completely fixed, but was not tender. The mass lay over the pelvic brim and transmitted pulsation from the iliac arteries. The liver and spleen were not palpable and no abnormality

FIG. 35.—Barium enema showing contracted cæcum with smooth, round, filling defect caused by argentaffin carcinoma of ileocæcal valve. A trace of barium occupies the orifice of the valve.

was found on rectal examination. The heart and lungs were normal and the blood-pressure was 170/110.

INVESTIGATIONS.—

*Blood-count*: Hæmoglobin 13·6 g. per 100 c.c. (92 per cent); R.B.C. 5,060,000/c.mm. W.B.C. 4400/c.mm.

*Blood-urea*: 50 mg. per 100 c.c.

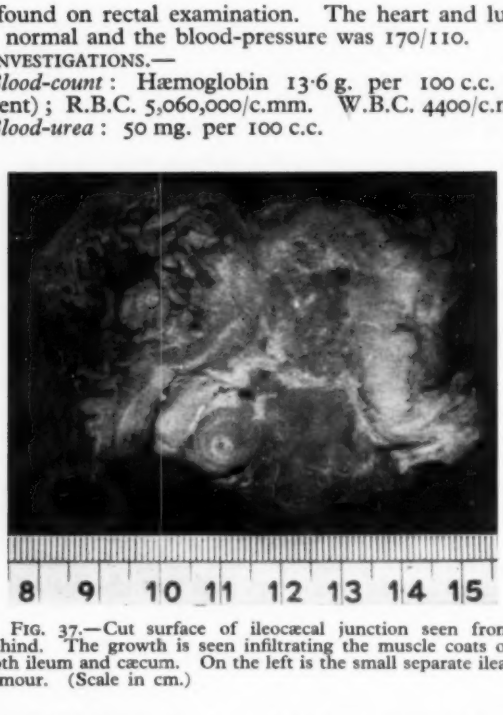


FIG. 37.—Cut surface of ileocæcal junction seen from behind. The growth is seen infiltrating the muscle coats of both ileum and cæcum. On the left is the small separate ileal tumour. (Scale in cm.)

*Radiological examination*: A barium enema showed a contracted cæcum with a smooth, round, filling defect at the site of the ileocæcal valve. No barium entered the small intestine (*Fig.* 35).

CLINICAL DIAGNOSIS.—Carcinoma of cæcum.

OPERATION (Feb. 25).—The abdomen was opened through a right paramedian incision. At the ileocæcal junction was a hard mass which was fixed to the posterior abdominal wall at the brim of the pelvis. No secondary deposits were found in the lymph-nodes, liver, or peritoneum.

The mass was mobilized with some difficulty and not without apprehension, as it was adherent to the iliac

FIG. 36.—Cæcum opened to show tumour of ileocæcal valve. The tip and base of the appendix are seen above and below the ileocæcal junction.

vessels. The right ureter could not easily be separated from the growth and its upper part was dilated. After palpating the left kidney a length of ureter was therefore resected, and as the ends could not be approximated they were ligatured. A right hemicolectomy was then performed, removing the lower 18 in. (45 cm.) of the ileum, the cæcum and ascending colon, and the proximal third of the transverse colon. The operation was terminated in the Mikulicz fashion by suturing the ileum to the transverse colon to form a spur and exteriorizing the bowel ends. A drain was inserted through a small incision in the right flank.

DESCRIPTION OF SPECIMEN.—On opening the cæcum a smooth hard mass measuring 4·0 × 3·0 cm. at its base was found to be projecting into the lumen for a distance of nearly 2·5 cm. The lumen was considerably reduced in size and was almost completely occupied by the mass. At the most prominent part of the mass lay the orifice of the ileocæcal valve. The growth involved only the posterior half of the orifice, which was converted from a horizontal to an almost vertical fissure. The terminal part of the ileum lay in front of the growth and was much reduced in calibre. Ulceration had not occurred (*Fig.* 36).

When sectioned, the tumour was seen to have penetrated the muscular coats of the ileum and cæcum to form a bulky mass in the retroperitoneal tissue and in the lower part of the mesentery. The overall dimensions of the tumour were 6·5 × 5·5 × 5·0 cm. Its cut surface was bright yellow in colour and was traversed by strands of pale-grey tissue (*Fig.* 37). The appendix could be followed backwards for 2·0 cm. from its base, after which it was lost in the retroperitoneal mass, from the upper part of which its tip re-emerged. Both recognizable parts of the appendix were extensively invaded by growth. The excised portion of ureter was stripped off the posterior aspect of the growth and on microscopical examination was found not to be invaded. The ileum was hypertrophied and dilated and 4·0 cm. above the ileocæcal valve there was a second yellow submucous tumour 1·0 cm. in diameter. It had penetrated the underlying muscle, but appeared to be separate from the larger tumour. Only one enlarged lymph-node was found in the specimen.

HISTOLOGY (Dr. C. F. Ross).—

*Blocks from Main Tumour Mass.*—Sections show the typical structure of argentaffin carcinoma. The tumour

is composed of well-defined masses of polyhedral cells with large nuclei having scattered chromatin in fine punctate masses, and abundant cytoplasm which in most places is filled with fine granules staining pink with eosin

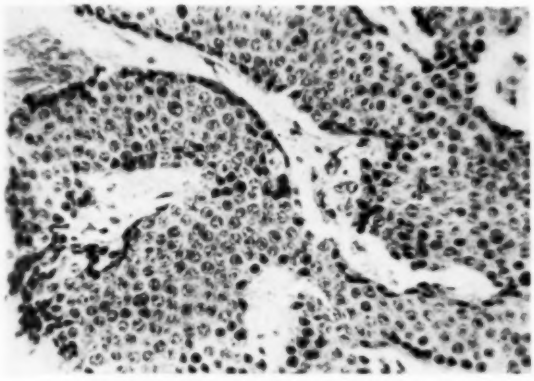

FIG. 38.—Main tumour mass. (× 235.)

and orange with van Gieson. In some areas there are small acini. Cell boundaries are rather indistinct and the masses are cut off by vascular fibrous trabeculæ into islands of various sizes, and there is a tendency for the peripheral cells to be rather flattened and to have nuclei with closer packed chromatin (*Fig.* 38). In parts, the cells in the centres of the masses are larger and less well pigmented than those more peripherally situated, and in places acinus formation is more marked than in others. On the whole, however, differentiation is fairly good. The tumour tissue has destroyed the whole thickness of the bowel wall and extended into the adjoining fatty connective tissues, with the production of a good deal of fibrosis and some chronic inflammatory reaction. It can be seen surrounding nerves and vessels, and here and there appears to be growing inside dilated lymphatics. Mitoses are not seen.

*Blocks from Adjacent Connective Tissues, Blood-vessels, and an Enlarged Lymph-node.*—Sections show invasion of the connective tissues by growth resembling the main mass. It is surrounding vessels and nerves, but there is no evidence of blood-vascular involvement. Many small lymphatics at some distance from the growth show masses of tumour cells in their lumens, and the lymph-node shows early invasion (*Fig.* 39). There is no evidence of growth in the ileocolic blood-vessels or small lymph-nodes present in the mesentery.

*Blocks from Ileal Nodule.*—Sections show a typical argentaffin carcinoma which is invasive and has spread throughout the ileal wall to form a small peritoneal nodule. There is no evidence of connexion between this and the main mass, and I think it is a separate tumour altogether.

*Special Staining Methods.*—The main tumour and the ileal nodule were investigated by the following methods. (*a*) Masson's silver method; (*b*) Clara's diazo method; (*c*) Periodic-acid-Schiff; (*d*) Sudan III and Sudan black (in frozen sections); (*e*) Ultra-violet microscopy (in frozen sections); (*f*) Schultz's reaction for cholesterol (in frozen sections); (*g*) Gibbs' reaction (darkening of the granules when treated with a buffered aqueous solution of 2 : 6-dichloro-quinone-chloroimide at *p*H 9·2).

The results were as follows and were given equally by both tumours :—

*a.* Very marked blackening of the granules with the silver diammine solution throughout the tissue, though more accentuated at the periphery of the masses as is usually the case (*Fig.* 40).

*b.* The granules give a positive diazo reaction. Though this is not as easy to see as the silver staining, the distribution is the same.

*c.* The specific granules give only faint pink staining, though this is deeper in frozen sections. Some parts of the tumour tissue show numerous small masses of strongly positively staining material in their cytoplasm, varying in

FIG. 39.—Lymph-node, showing early metastasis. (× 95.)

size from just visible granules to masses 20 μ in diameter. Where there are acini, the lumen contains P.A.S.-positive material. These masses are quite distinct from the argentaffin granules.

*d.* Sudan III shows numerous small granules, larger and distinct from the argentaffin granules, which stain rather poorly. Sudan black, however, stains them very well. They are coarse and evenly distributed throughout the tumour cells, even where the specific granules are scanty, and do not correspond to the P.A.S.-positive material.

*e.* Frozen sections of the tumour show slight but definite fluorescence with ultra-violet light.

*f.* Schultz's reaction is negative.

*g.* Gibbs' reaction is positive.

FURTHER PROGRESS.—This was uneventful for two weeks, after which a watery discharge from the flank

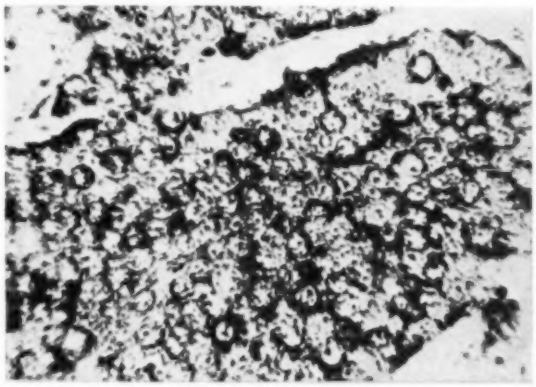

FIG. 40.—Main tumour mass, showing argentaffin granules. (× 390.)

incision commenced. An excretion urogram showed no secretion by the right kidney, and lipiodol injected into the fistula demonstrated an irregular cavity deep to the abdominal wall but no communication with the urinary tract. As the discharge showed no sign of abatement, a right nephrectomy was performed on April 20. An oblique loin incision was used and a dilated kidney and 4 in. (10 cm.) of ureter were removed. The discharge ceased immediately.

After crushing the spur the ileocolostomy was closed extraperitoneally on May 2, and the patient left hospital on May 16. He slowly regained his normal weight and resumed work as an engineer in September. He was

*Table I.*—ARGENTAFFIN CARCINOMATA OF THE ILEOCÆCAL VALVE

| CASE No. | AUTHOR | DATE | AGE | SEX | LENGTH OF HISTORY | CLINICAL FEATURES | RADIOLOGY | PRIMARY TUMOUR | METASTASES | TREATMENT | RESULT |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Dukes and Lockhart-Mummery | 1926 | 76 | F. | 1 yr. | Indigestion and occasional sickness. Mass | — | Posterior margin ileocæcal aperture | Present | Resection | Recovered |
| 2 | Carr | 1931 | 61 | M. | — | Attacks of abdominal pain and diarrhœa. Mass | Filling defect cæcum | 4 cm. diam. Pedunculated. From posterior margin of valve | Absent | Resection | Recovered |
| 3 | Ariel | 1939 | 54 | M. | 20 yr. | Diarrhœa. Pain in R.I.F. Mass | Irregularity of terminal ileum. Filling defect cæcum | Almost encircled valve | Present | Resection | Well after 6 months |
| 4 | Mallory | 1940 | 78 | M. | 2½ yr. | Attacks of abdominal pain and diarrhœa | Deformity of cæcum at ileocæcal valve | Primarily involved ileocæcal valve | — | Resection | Recovered |
| 5 | Terplan, Weintraub, and Wolf | 1940 | 60 | M. | — | Abdominal cramps. Constipation | Adhesions about cæcum | Involved ileocæcal valve | Present | Ileosigmoid anastomosis | Well 5½ yr. Accidental death |
| 6 | Dockerty and Ashburn | 1943 | 63 | F. | Several years | Abdominal cramps. Mass | 'Carcinoma in region of ileocæcal valve' | 3 × 3 × 2 cm. | Present | Resection | Well after 2 years |
| 7 | Dockerty and Ashburn | 1943 | 63 | M. | 3 mth. | Recurrent abdominal cramps and vomiting | Lesion of terminal ileum | 3 × 2 × 2 cm. | Present | Resection | Well after 15 months |
| 8 | McLeod | 1944 | 66 | F. | 6 mth. | Diarrhœa | Enema normal | 2·2 × 1·8 × 1·5 cm. Perforation of cæcum | Present | No operation | Death from peritonitis |
| 9 | Horn | 1949 | 68 | F. | — | 'Partial intestinal obstruction'. Mass | — | 3 cm. diam. | Present | Resection | Well after 4 years |
| 10 | Horn | 1949 | 46 | F. | 1 yr. | Episodes of vomiting | Filling defect cæcum | 3 cm. diam. Polypoid. Superior lip of valve | Present | Resection | Recovered |
| 11 | Gallart Mones, Valls Colomer, and Vilar Bonet | 1950 | 63 | M. | 1 yr. | Attacks of pain, vomiting, and diarrhœa | Filling defect cæcum | 3·5 cm. diam. Completely surrounded valve | Present | Resection | Died after 3 years |
| 12 | Ross | 1952 | 85 | F. | 6 wk. | Pain. Diarrhœa. Mass | Barium meal normal | 2·5 cm. diam. Upper lip of valve | Present | No operation | Died after 7 weeks |
| 13 | Le Brun (present case) | 1953 | 57 | M. | 4 yr. | Attacks of abdominal pain and vomiting. Constipation. Mass | Filling defect cæcum | 4·0 × 3·0 × 2·5 cm. Posterior part of valve | Present | Resection | Well after 3 years |

last seen in June, 1953, and had no complaints apart from the passage of two rather loose stools daily. Some induration was still palpable beneath the paramedian scar. This had not altered since the wound healed and appeared to be the result of multiple procedures at this site.

Neither naked-eye nor histological examination of the tumour enabled a decision to be made as to whether it arose primarily in the ileocæcal valve or in the appendix, as both structures were involved. As already mentioned, appendicular argentaffin carcinomata rarely spread beyond the appendix and in none of the 18 cases in which this has occurred has the ileum or the cæcum been invaded. On the other hand, 12 cases have been described in which the tumour undoubtedly arose at the ileocæcal valve. The pathological and clinical features of these cases bear a distinct resemblance both to each other and to the present case, which has therefore been diagnosed as an argentaffin carcinoma of the ileocæcal valve.

## ARGENTAFFIN CARCINOMATA OF THE ILEOCÆCAL VALVE

*Table I* gives the main features of the 13 cases and further details are as follows :—

**Pathology.—**

*The Primary Tumour.*—That the growth formed a rounded, nodular, or polypoid projection into the cæcum is described in 8 cases, and that 2 further cases had this characteristic is suggested by a filling defect demonstrated radiologically. In 1 case (*Case* 9) the growth was confined to the ileal side of the valve. Evidence of obstruction of the valve was noted in 11 cases. Ulceration is mentioned in 6 cases only. In 5 it was superficial, but in *Case* 8 it proceeded to perforation of the cæcum. Perforation at the site of an argentaffin carcinoma is also described by Stewart and Thomson (1951). The colour is given as yellow, orange, or brown in 9 cases. Multiple tumours were present in 3 cases (*Cases* 3, 7, and 13), the additional growths occurring in the ileum, appendix, cæcum, and ascending colon.

*Metastases* occurred in 11 cases, in all of which the regional nodes were involved. In 3 cases there were secondary deposits in the liver, and in 1 (*Case* 12) there were widespread metastases. Penetration of the bowel wall with proliferation in the mesentery and pericolic areolar tissues occurred in 8 cases.

*Histology.*—No unusual histological features were described in the series. The argentaffin reaction was carried out in 8 cases and was positive in 7. It was negative in *Case* 12 and Ross (1952) discusses the possible reasons for this.

**Clinical Features.**—The ages ranged from 46 to 85 years, the average being 65. There were 7 males and 6 females. Gastro-intestinal symptoms occurred in every case and in 7 had been present for 1 or more years. In most cases they were notably intermittent and consisted of bouts of colicky abdominal pain, vomiting, and diarrhœa, either singly or in combination. Despite the high proportion of cases in which the growth was found to obstruct the ileum, constipation is mentioned in only 2 cases, and in only 4 was there clinical evidence of intestinal obstruction. Blood was recognized in the stools in 1 case only. Loss of weight occurred in 7 cases. A mass was palpable in the right iliac fossa in 7 cases, in most of which proliferation of the growth outside the bowel wall, or enlarged glands in the ileocæcal angle, contributed significantly to the size of the mass.

**Special Investigations.—**

*Tests for Occult Blood* in the stools were carried out in 2 cases only. In *Case* 4 they were negative, and in *Case* 12 only one of three specimens was positive.

*Radiological Examination.*—This was carried out in 11 cases and in 6 a filling defect in the cæcum was demonstrated. Radiographs have been reproduced with only one of the recorded cases (*Case* 11) but they bear a striking resemblance to those of the author's case. In both the cæcum is notably contracted and there is a smooth, round, filling defect at the site of the ileocæcal valve.

Contraction of the cæcum seems to be of diagnostic importance in this tumour as there is evidence that it occurred in three other cases. In *Case* 4 the barium enema showed " a considerable area of narrowing and deformity in the region of the ileocæcal valve ", though no filling defect was demonstrable ; in *Case* 5 radiography suggested adhesions about the cæcum, though none are mentioned in the account of the operation, while the description of the specimen in *Case* 8 states that " the cæcum was contracted and its inner wall drawn together ". This effect appears to be the result of the fibrosis which is associated with penetration of the wall of the bowel and proliferation of the growth in the subserous and retroperitoneal tissues. It is thus comparable to the kinking produced by argentaffin carcinomata of the jejunum and ileum.

The author's case shows the desirability of performing an excretion urogram before exploring tumours of the ileocæcal region.

*Hæmoglobin.*—This is given in 5 cases, the average figure being 13·4 g. per cent. In *Case* 12, which had widespread metastases, it was 9·9 g. per cent, but in the other cases was within normal limits.

**Diagnosis.**—The clinical diagnosis in 8 cases was carcinoma of the cæcum. *Case* 3 was diagnosed as regional ileitis with involvement of the cæcum. The patient was under the personal care of Dr. Burrill B. Crohn at the Mount Sinai Hospital, New York. In addition to the tumour at the ileocæcal valve there were ten separate tumours in the lower part of the ileum and several small nodules in the cæcum and ascending colon. Crohn (1949) states that argentaffin carcinomata of the terminal ileum may simulate the ' string sign ' of regional ileitis.

**Treatment.**—*Resection* was performed in 10 cases. One case (*Case* 11) died after three years but there was no autopsy. The remainder were well when reported, 5 in the first year, and 1 in each of the second, third, fourth, and fifth years after operation.

*Anastomosis only* was performed in *Case* 5, as the primary growth was fixed and there were secondary deposits in the regional nodes and liver. The patient remained well for five and a half years and then met an accidental death. Post-mortem examination failed to reveal any increase in the size and extent of the tumour or its metastases.

## DISCUSSION

**Diagnosis.**—From the foregoing analysis it would appear justifiable to make a tentative diagnosis of argentaffin carcinoma of the ileocæcal valve in a middle-aged or elderly patient who has suffered from recurrent gastro-intestinal disturbances over a period

of a year or longer, and in whom a barium enema shows a contracted cæcum with a smooth, round, filling defect at the site of the valve. The diagnosis would become more certain if diarrhœa were present, if there was no anæmia, and if occult blood were absent from the stools or present only in traces. In a recent review of 140 cases of adenocarcinoma of the right colon, Person and O'Neill (1950) found that the average duration of symptoms was nine months, the hæmoglobin averaged 10·9 g. per 100 c.c., and occult blood was present in the stools in 80 per cent.

**Metastases.**—Although the figures are too small for accurate comparison, they suggest that metastases occur more frequently from argentaffin carcinomata of the ileocæcal valve (85 per cent) than from similar tumours occurring elsewhere in the gastro-intestinal tract (*Table II*). That the comparison may be a true one, however, is suggested by the fact that *all* the ileocæcal valve growths caused symptoms which drew attention to their presence, while many growths elsewhere remain silent. In Person and O'Neill's series of adenocarcinomata of the right colon metastases were not present in more than 53 per cent.

*Table II.*—Metastases from Argentaffin Carcinomata at Various Sites Exclusive of Appendix

| Site of Primary Growth | Number of Cases | Number of Cases with Metastases | Percentage with Metastases |
|---|---|---|---|
| Ileocæcal valve | 13 | 11 | 85 |
| Cæcum | 21 | 11 | 50 |
| Colon | 7 | 3 | |
| Jejunum and ileum | 237 (Ariel, 1939) | 59 | 25 |
| Stomach | 24 | 5 | 21 |
| Rectum | 80 | 9 | 11 |
| Duodenum | 14 | 1 | 7 |

**Treatment.**—The treatment of argentaffin carcinomata of the ileocæcal valve differs little from that of adenocarcinoma of the cæcum. A complete right hemicolectomy is preferable to any more limited type of resection in view of the tendency of the growth to metastasize.

If the primary tumour is inoperable the ileum should be divided and the proximal end anastomosed to the transverse colon. A biopsy should also be obtained to confirm the diagnosis, after which a better prognosis can be given than with an adenocarcinoma of similar extent. In all cases the whole of the gastro-intestinal tract, and particularly the jejunum and ileum, should be examined for additional tumours.

## SUMMARY

The literature referring to the malignancy and clinical features of argentaffin carcinomata is reviewed.

A tumour of this nature arising at the ileocæcal valve is described, and a series of similar cases is discussed. They give a more characteristic clinical picture and metastasize more frequently than argentaffin carcinomata elsewhere in the gastro-intestinal tract.

I wish to thank Mr. G. A. Bagot Walters, of Lincoln, for permission to describe the case; and Dr. C. F. Ross, of St. Peter's Hospital, Chertsey, for the histological report and photomicrographs.

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# PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY IN THE DIAGNOSIS OF OBSTRUCTIVE JAUNDICE

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CHOLANGIOGRAPHY, by the direct introduction at operation of contrast media into the main biliary duct or post-operatively through a tube inserted at operation, is a valuable and increasingly common procedure. Radiological demonstration of the biliary duct system apart from operation has not been generally regarded as practicable. Isolated attempts have, however, been made, and Lee (1942) and Royer and Solari (1947) obtained cholangiograms by the injection of contrast media into the gall-bladder under peritoneoscopic control. These attempts do not appear to have been followed up, presumably because it was felt that the danger of biliary leakage was too great. More recently, Carter and Saypol (1952) have described a case of obstructive jaundice in which cholangiograms were obtained by needling the left lobe of the liver under general anæsthesia, and injecting the contrast medium after identifying an intrahepatic biliary duct by aspiration.

This transhepatic approach appeared to offer the possibility of development into a routine clinical test and we are herewith reporting 3 cases of obstructive jaundice in which the method was successfully used, and 1 case in which it was technically successful but in which a serious complication in the form of intraperitoneal bleeding and biliary leakage occurred which led to the death of the patient. The factors thought to be responsible for this fatal result and the possibility of their avoidance in the future will be discussed. These cases plus three control cases represent all the cases in which we have attempted the method to date. In addition Mr. T. H. Cullen, of Kettering, has successfully employed the same technique, and we are grateful to him for allowing us to report the case.

## TECHNIQUE

The procedure was performed on in-patients, in the X-ray department, after a preliminary injection of morphine. The site selected for injection was the anterior abdominal wall close to the right costal margin and about 1½ in. to 2 in. from the ensiform cartilage. This area was anæsthetized with 2 per cent novocain and a graduated needle, 12 cm. long and 1 mm. in external diameter, fitted with a sight feed and stylet, was introduced backwards, slightly upwards, and to the right until it was felt to enter the liver. This was confirmed by noting that the needle moved with respiration. The stylet was then removed and a 20-ml. syringe containing saline connected by a rubber tube fitted with adaptors. The needle was slowly advanced while an assistant maintained suction on the syringe. When, as frequently happened, a portal radicle was entered, the blood was washed out of the sight feed by injecting a few ml. of saline. Suction was also maintained during withdrawal of the needle. If no bile was detected, the needle was reinserted in a slightly different direction, the stylet being occasionally inserted to make sure that the needle was not blocked. When a bile-duct had been located, a few ml. of 35 per cent diodone were injected and a check radiograph taken to confirm that the biliary tree was filling. Twenty ml. of 35 per cent diodone was then injected slowly under screen control and the needle withdrawn. A series of radiographs was then taken, including some in the erect posture.

Bile was usually aspirated at a depth of between 5 cm. and 7 cm. from the skin. In *Cases* 1 and 4, the actual entry of the needle into a bile-duct could be felt distinctly, but the sensation was in no way different from that given by puncture of a portal radicle. In the remaining cases successful biliary puncture gave no special sensation and was revealed only by aspiration. Most difficulty was experienced in *Case* 2, four needlings being required before bile was aspirated; in this case, however, an earlier successful tap had been disregarded as the nature of the white bile withdrawn was not immediately recognized.

In all four cases of obstructive jaundice in which we have used the procedure good and diagnostic X-ray pictures were obtained. No pictures were obtained in two control cases in which jaundice was not present, nor were we successful in one other non-jaundiced patient in whom we made the attempt by needling the liver at operation. Brief histories of the successful cases are given below together with that of the case in which the method was technically successful but in which the patient subsequently died, and also of Mr. Cullen's successful case.

## CASE REPORTS

*Case* 1.—This was a woman aged 65 with a six-weeks' history of abdominal pain, at first diagnosed as due to gall-stones, and a one-week's history of jaundice. The rapid deterioration in the patient's general condition in the short time before her admission led to the suspicion of malignancy. Peritoneoscopy was performed (Mr. R. S. Handley), and the liver and gall-bladder were found to be normal in size. Peritoneoscopic biopsy of a white nodule in the right lobe of the liver revealed a columnar-celled mucoid adenocarcinoma. It was decided to attempt percutaneous transhepatic cholangiography with the results shown (*Figs.* 41, 42). It will be seen that the obstruction is high up in the hilum of the liver immediately distal to the junction of the right and left hepatic ducts. No operative palliative procedure seemed feasible, the patient's condition continued to deteriorate rapidly, and she died three weeks later. No post-mortem was obtained.

*Case* 2.—This was a man, aged 50, with a four-months' history of abdominal pain and jaundice associated with loss of weight. On examination a distended gall-bladder could be felt and the liver was also enlarged. Full chemical investigations were carried out, the details of which do not bear on the present report; but it may be stated simply that the results pointed to an obstructive jaundice. Percutaneous transhepatic cholangiography was performed and showed an obstruction at the lower end of the common bile-duct (*Fig.* 43).

Operation was performed and a hard mass 1 in. to 1½ in. in diameter was found surrounding the common bile-duct immediately above the duodenum. The portal vein and hepatic artery were also involved in the mass. A diagnosis of carcinoma of the common bile-duct was made and it was decided that the growth was irremovable surgically. As the growth extended to immediately below the level of the entry of the cystic duct it was decided that an anastomosis to the gall-bladder might fail to relieve the jaundice for long. The jejunum was therefore divided and an anastomosis-in-Y performed between the distal cut end of the jejunum and the dilated common hepatic duct above the growth. The post-operative course was straightforward, and the patient discharged relieved of his jaundice.

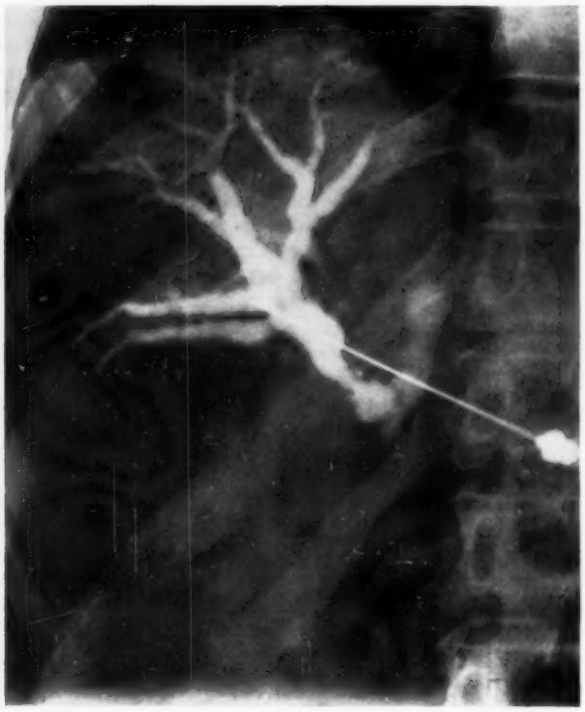

FIG. 41.—*Case* 1. Needle in position after injection of 10 ml. 35 per cent diodone. Showing dilated right hepatic duct, early filling of left hepatic duct, and obstruction just below their junction.

FIG. 42.—*Case* 1. After injection of 20 ml. 35 per cent diodone and withdrawal of needle. Film taken in erect posture, showing grossly dilated biliary tree and an irregular obstruction of the upper part of the common hepatic duct.

*Case* 3.—This was a man, aged 75, with a three-weeks' history of pain and diarrhœa. His doctor when called in noticed that the patient was jaundiced. On examination, he was a thin anæmic elderly man with a palpable distended gall-bladder. On admission to hospital and without any preliminary treatment by vitamin K, percutaneous transhepatic cholangiography was performed using 20 ml. diodone as in the first two cases. A good X-ray picture of dilated intrahepatic bile-ducts was obtained, but the test was repeated after two days using 40 ml. diodone to obtain more complete filling of the very dilated ducts. This again was successful and an irregular tapering obstruction of the lower end of the common bile-duct was shown (*Fig.* 44), diagnosed as due to carcinoma of the head of the pancreas.

Following this second procedure he complained of abdominal pain, and subsequently vomited and complained of pain in the left shoulder, though this last symptom was rendered more difficult to interpret by the fact that he had recently fallen and bruised his left shoulder. He was given two pints of blood, but the abdomen gradually became more prominent, jaundice more marked, and anuria developed; the last was treated by measured fluid replacement.

On the third day after the second needling of the liver, a limited exploration of the abdomen was carried out under local anæsthesia through the right iliac fossa; 45 oz. of predominantly blood-stained fluid, but with also a biliary tinge, was evacuated; in addition, it was estimated that about 10 oz. escaped unmeasured. The abdominal cavity was drained. The patient did not rally and died some hours later.

At post-mortem the diagnosis of carcinoma of the head of the pancreas was confirmed. The needle puncture of the liver from which the fatal leak had occurred was minute.

*Case* 4.—This was a man of 72 with a three-weeks' history of increasing painless jaundice. On examination he was wasted and deeply jaundiced, with an enlarged liver; the gall-bladder was not palpable. Barium studies of the duodenum showed no mucosal distortion or widening of the duodenal loop. After preparation with vitamin K for five days the prothrombin time was within normal limits (17 seconds). Transhepatic cholangiography was performed.

The radiograph (*Fig.* 45) showed a dilated biliary tree and common bile-duct, the lower part of which appeared to be distorted and narrowed as though by extrinsic pressure. A diagnosis of carcinoma of the head of the pancreas was made.

Peritoneoscopy (Mr. R. S. Handley) was performed 2 hours after the cholangiography, and there was no blood or bile in the peritoneal cavity. The site of the needle puncture was inspected and found to be sealed by a bead of clot from which a thread of fibrin stretched across the air-filled peritoneal cavity to the puncture in the anterior abdominal wall.

At laparotomy a growth was found in the head of the pancreas encircling not only the common bile-duct but also the portal vein. Choledochoduodenostomy was performed. The patient died one week later of renal failure. There was no post-mortem.

*Case* 5.—This was a man of 63 who was admitted to Kettering General Hospital under the care of Mr. T. H. Cullen with a three-months' history of increasing jaundice, abdominal pain, and loss of weight. On examination the patient was deeply jaundiced, with a palpable liver and gall-bladder. After preparation with vitamin K, percutaneous cholangiography was performed, white bile being aspirated at the initial puncture. The site of the obstruction was shown to be in the common bile-duct. It is interesting to note that after half an hour the diodone began to outline the gall-bladder and the dye accumulated there (*Fig.* 46) until at twenty-four hours the hepatic ducts were empty and the gall-bladder alone showed on the radiograph.

At operation a fixed growth was found involving the head of the pancreas, duodenum, and pyloric end of stomach. Cholecystgastrostomy was performed. The site of needle puncture of the liver could be identified, but there was no evidence of bleeding, hæmatoma, or extravasation of bile.

FIG. 43.—*Case* 2. Radiograph (oblique view) taken in the erect position after injection of 20 ml. 35 per cent diodone and removal of needle. A trace of dye has entered the gall-bladder (indicated as thin line running down from the lower end of obstructed common bile-duct with small pool of dye in fundus of gall-bladder below level of crest of ilium). Complete obstruction of the common bile-duct was confirmed at operation.

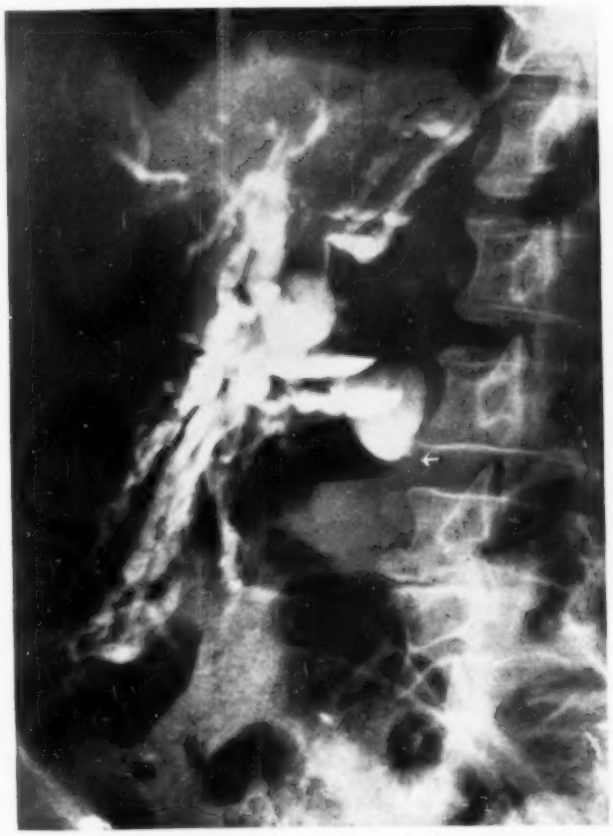

FIG. 44.—*Case* 3. Oblique radiograph taken in the erect position after injection of 40 ml. of 35 per cent diodone. The fluid levels show that even this quantity has failed to fill completely the enormously dilated common bile-duct. The arrow indicates irregular obstruction of its lower end.

## DISCUSSION

The cases herewith reported show that percutaneous transhepatic needling of the liver with injection of diodone is capable in cases of obstructive jaundice of giving excellent and often diagnostic X-ray pictures. The negative control cases also suggest that without the dilatation of the intrahepatic ducts of chronic obstructive jaundice, filling and radiography of the biliary system are unlikely. Since the differentiation of obstructive from other types of jaundice is often difficult in spite of full clinical and biochemical investigations, a test which is capable of establishing the diagnosis of obstructive jaundice as well as the site and probable nature of the obstruction is obviously potentially valuable. The details of the intra- and extrahepatic biliary duct systems should be of particular value in planning operative treatment in cases of chronic jaundice due to operative trauma to the biliary ducts. But the value of any test is related to the risks, and in this connexion *Case* 3, in which the test led to the death of the patient from intraperitoneal leak, is crucial to a decision on its value. We feel, however, that through inexperience we made avoidable mistakes in this case which may have been responsible for the fatal complication, in particular by our failure to prepare the patient before the test with vitamin K. We have now adopted the routine of treating these patients with vitamin K and not carrying out the test until the prothrombin readings are satisfactory. Since the fatal result followed the injection of 40 ml., we are also limiting for the present the amount of diodone injected to 20 ml. Should there be in spite

of these precautions clinical evidence of serious leak, we now feel that early laparotomy should be done either to drain the peritoneal cavity or to carry out the definitive operation indicated. The test should therefore tentatively be regarded as comparable to other tests such as air encephalography in which

FIG. 45.—*Case* 4. Radiograph taken in the supine position after injection of 20 ml. of diodone, showing dilated duct system with irregular narrowing and distortion of the lower end of the common bile-duct as though by extrinsic pressure. The diagnosis of carcinoma of the head of the pancreas was confirmed at operation.

real dangers exist and are recognized, but are countered by an attitude of watchful expectancy with urgent operation if indicated.

The dangers of intraperitoneal bleeding and biliary leakage must exist in all cases of needling of the liver, but should not be greater in the passage of a narrow bore needle for cholangiography than of a stouter needle for liver biopsy, but rather the reverse. Large series of cases of successful liver biopsies have been published (Terry, 1949). We therefore suggest that in spite of our fatal case, the procedure of percutaneous transhepatic cholangiography is worthy of cautious further exploration as a companion test to liver biopsy in the diagnosis of chronic jaundice.

## SUMMARY

1. A technique for percutaneous transhepatic cholangiography is described.

2. In 4 cases of obstructive jaundice the procedure was technically successful and clinically uneventful.

3. In 1 further case of obstructive jaundice, the procedure was technically successful but led to the death of the patient from blood and biliary leakage into the peritoneal cavity. We attribute this fatality largely to the failure to prepare the patient for the test with vitamin K.

FIG. 46.—*Case* 5 (Mr. T. H. Cullen's case). Radiograph taken one hour after injection of 20 ml. 35 per cent diodone, showing the gradual disappearance of dye from the duct system and its collection in the gall-bladder. Earlier films (not reproduced here) had demonstrated obstruction of the common bile-duct.

4. In 3 cases without obstructive jaundice, in 1 of which the liver was needled at operation, the procedure was unsuccessful.

5. We feel that in spite of the fatal case, a cautious further exploration of the procedure is justifiable.

We wish to acknowledge our indebtedness to Mr. R. S. Handley for allowing us to carry out the test on *Case* 4, and for kindly performing the peritoneoscopies in *Cases* 1 and 4; also to Mr. T. H. Cullen for allowing us to publish the details of his case.

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# CHRONIC LYMPHŒDEMA OF THE EXTREMITIES AND ITS MANAGEMENT

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CHRONIC lymphœdema is a condition which has proved extraordinarily intractable to treatment, and, since the attempts of Lisfranc in the nineteenth century to treat the disease by scarification (1841) and multiple puncture (1845), the numerous procedures devised bear witness of its resistance to surgical relief. The disabling and unsightly nature of the condition may reduce an otherwise young and healthy patient to a state of semi-invalidism. On account perhaps of its comparative rarity, informative literature on the subject is somewhat sparse, and the matter is dealt with rather summarily in most standard text-books.

It is felt, therefore, that a general survey of the condition, and an indication of how far these patients can be helped by surgical treatment, may be of value. This paper is based on a series of 26 cases observed at the Queen Victoria Hospital, East Grinstead, during the past five years. Of this series of cases, 4 were treated conservatively, 6 have remained under observation following operations of the Kondoléon type, and the remainder were treated by the surgical measures later described.

As with other circulatory disorders of the extremities, the condition presents both static and dynamic aspects, and it is necessary to consider not only the visible pathological changes occurring in the limb, but also the concurrent failure in drainage of the extravascular fluid. Our knowledge of both aspects is regrettably incomplete, since the aetiology is obscure in a high proportion of cases, and also much remains to be learned of the dynamics of lymph-flow, and of the formation and removal of tissue fluid. The anatomical and physiological features of lymph-drainage are important in forming a conception of the possibilities of treatment, and merit a brief review of some of the salient points.

## ANATOMICAL, PHYSIOLOGICAL, AND PATHOLOGICAL CONSIDERATIONS

The lymphatic circulation of the skin (Gray, 1939) takes place in a closed system of vessels, which arise peripherally as a superficial plexus lying in the immediate subepithelial region of the dermis; this plexus is valveless and continuous over the whole surface of the body. From this plexus lymph drains through larger collecting vessels running perpendicularly or obliquely through the dermis, and showing the first appearance of valves at or near their junction with the deep plexus. The subdermal plexus, which lies at the level of the junction of dermis with superficial fat, is a series of valved collecting radicles rather than a true plexus. These radicles drain into larger collecting trunks, lying in the subcutaneous fat near to the deep fascia of the limb, but not necessarily in close association with it. In addition to valves the larger trunks are provided with muscular walls, and it is evident that drainage becomes an active rather than a passive process as lymph passes from the smaller to the larger vessels in its transit to the regional glands. Kinmonth (1952) has recently shown with dye injection studies that the normal lymph-flow is more rapid than can be explained by diffusion, compressive effects of surrounding tissues, or capillarity, and suggests that it is the initial state of emptiness of the trunks which aids the astonishingly rapid passage of dye along them when this is injected at the periphery of the normal lymphatic tree.

The capacity of the superficial plexus alone for the transmission of lymph from one area to another is very limited, and the flow in the collecting trunks is unidirectional, so that obstruction of one section produces a corresponding zonal stagnation of lymph, which can only be relieved by percolation of the excess fluid through the subcutaneous tissues under the influence of gravity, until an intact collecting tree is encountered. There are no significant connecting channels passing through the deep fascia of the limb, and beneath this layer the appearance of the tissues is normal in the lymphœdematous limb; no conclusive facts are known, however, regarding the patency in chronic lymphœdema of lymphatic pathways beneath the deep fascia, which have usually been assumed to be functioning normally, a presumption which formed the basis of the Kondoléon operation (1912). It is conceivable, however, that as the thickened deep fascia in these cases forms such a perfect and inelastic support for the underlying structures, macroscopical changes might well not be apparent even in the presence of an obstructed deep system. The secondary pathological changes probably only occur where fluid stagnates in the distensible subcutaneous spaces. The rapid rise in tissue pressure in the muscular compartments of the limb prevents pooling of fluid beneath the deep fascia.

Drinker and Yoffey (1941) have shown that one of the principal functions of lymphatic flow is the conveyance of protein, which is constantly escaping from the blood capillaries into the tissue spaces, back into the general circulation. It is generally agreed that lymphœdema basically arises from proximal obstruction of the lymphatic collecting tree of the limb, leading to distal stagnation of fluid of high protein content in the tissue spaces. Estimations of the total protein content (less fibrinogen) of fluid obtained at operation in the limbs of 5 patients in the series under review, gave results of 5·23, 1·25, 5·75, 2·25, and 2·75 g. per cent, figures considerably in excess of what has been estimated to be the protein content of normal human tissue fluid; it is assumed that under conditions of stagnation the lymph and tissue fluid, separated by a lymph-vessel wall freely permeable to protein, reach approximate equality in protein content. The accumulation of protein molecules which have escaped from the blood capillaries, and possibly also of those resulting from cellular

catabolism, deranges the normal osmotic pressure relationship and impedes re-entry of fluid into the blood circulation. There is no evidence that electrolyte interchange is affected. McInally, Campbell, Robertson, and Douglas (1952) have recently studied the clearance of radio-sodium from the subcutaneous tissues of normal and lymphœdematous legs and have found that removal depends on the patency of the venous return rather than on the lymph circulation. It might be expected that the smaller albumen molecule would escape more readily than the globulin through the blood-vessel wall, giving rise to a higher osmotic pressure per gramme of protein in the tissue fluid than in the blood-plasma, but few observations appear to have been made in this connexion. In 3 cases in the series the A/G ratio of lymph collected from the affected limb was estimated and gave results of 6·6 : 1 in the first case, 2·3 : 1 in the second (plasma ratio 1·6 : 1), and 3·1 in the third (plasma ratio 2 : 1). Such isolated observations are not significant, but further investigation by the newer methods now available of the nature and size of the protein molecules present might prove illuminating; whether partial disintegration of protein molecules takes place during stagnation, producing further osmotic imbalance, is not known. There is an evident contrast between the softer œdema of venous insufficiency with electrolyte filtration into the interstitial space but with normal protein clearance, and the more solid lymphœdema with colloid retention. Certainly the external pressure required to empty the limb and to maintain its reduced size is greater in lymphœdema.

While the resultant stagnant fluid accumulates in the subcutaneous tissues, the limb swells and in due course local tissue reactions in fascia, fat, and skin take place. A network of dense fibrous tissue is laid down in interlacing fashion in the subcutaneous fat; the fat lobules become at first œdematous and hypertrophied, but later compressed and atrophic between the multiplying and proliferating fibrous strands. Fibrous tissue is particularly dense in the vicinity of the deep fascia, which is correspondingly thickened and gradually converted into a dense layer of scar tissue often 1 cm. in depth. The skin, at first stretched, gradually thickens from proliferation of fibrous tissue in the dermis; the epidermis becomes thickened and hyperkeratotic, and is subject to vesiculation, weeping, and infection, but ulceration is rare. As Mowlem (1948) has pointed out, in the lower limb the secondary changes in the superficial tissues tend to show an uneven distribution, the most advanced changes being in the distal part of the limb where stagnation is greatest. In long-standing cases warty papillomatous excrescences often develop on the skin. The œdematous tissues show a poor local resistance to infection with a tendency to erysipeloid skin reactions, diffuse underlying cellulitis, and severe constitutional disturbance. Such inflammatory attacks occur apparently spontaneously, and in susceptible cases repeatedly, each aggravating the condition further; in other cases these attacks occur infrequently or not at all.

Cases of acquired lymphœdema of whatever aetiology appear to have one factor in common—namely, the destruction of glands or lymphatic collecting trunks over an area sufficiently extensive to preclude regeneration; this is usually also associated with the extensive laying down of scar at the site of obstruction, which in turn serves to discourage re-anastomosis; Gray (1940) demonstrated the inimical effect of scar tissue on the sprouting by which anastomosis is achieved. The question of the patency or capacity for functional recovery of the peripheral collecting tree distal to the obstruction has a fundamental bearing on the possibility of surgical cure. Although large endothelial-lined spaces, often of considerable length, and containing quantities of lymph, can frequently be demonstrated at operation in cases of chronic lymphœdema, it has not been found possible to demonstrate an active centripetal flow in cases investigated in this series—injection of the dye disulphone blue V.N. intradermally after the method of Hudack and McMasters (1933) has shown only stagnation in dilated skin lymph capillaries. After subcutaneous injection just before operation, the dye has been found pooled near the injection site without evidence of passage along functional trunks. By direct injection of dye on two occasions into the large 'lymph-sinuses', disclosed at operation, it has been found possible to delineate a network of dilated lymphatic pathways from knee to ankle, the dye-stained fluid flowing in retrograde fashion toward the periphery when the limb was dependent, and proximally when elevated. Such movement, however, was purely passive in character and quite unlike the rapid unidirectional passage of dye along a normal lymph-trunk.

## CLASSIFICATION

The following clinical classification is based on the aetiology of the condition so far as this is known and has been found convenient, and there is little difficulty in placing cases under one of the headings described. The figures represent the distribution of cases in this series. :—

1. Congenital (1) and/or familial (1).
2. Lymphœdema præcox (18).
3. Infective lymphœdema :—
   *a*. Filarial (1).
   *b*. Non-specific inflammatory (1).
   *c*. Syphilitic or tuberculous (0).
4. Secondary to destruction of glands or trunks by :—
   *a*. Malignant involvement (0).
   *b*. Surgical extirpation and/or irradiation (3).
5. Traumatic.
6. Reflux chylous lymphœdema (1).

This scheme of classification excludes certain œdematous conditions in which the aetiological role of vascular as opposed to lymphatic deficiencies is in doubt. Such conditions include the 'white leg' of thrombophlebitis, or the chronic œdema following injuries in the region of joints. There seems little doubt that in œdema resulting from femoral or iliac thrombophlebitis, lymphatic stasis exists at least in the early stages of the condition, and is probably associated with periphlebitis; if, however, the condition becomes chronic, the picture resolves mainly into one of chronic venous insufficiency, and as such is outside the scope of this paper.

**1. Congenital Lymphœdema.**—Milroy (1892) originally described cases of lymphœdema arising as

both a congenital and hereditary affection. Such a condition is very rare, and in many cases described as 'Milroy's disease' does not fulfil these two criteria. Lymphœdema uncommonly occurs as a familial disorder, and more frequently as a sporadic congenital condition. It then presents as a smooth uniform enlargement of the limb present at birth. The health of the child is otherwise good. There are sometimes associated nævoid changes in the skin. The external genitalia may be affected when the lower limb is involved (*Fig.* 47). In upper limb involvement there may be associated lymphangiectatic cysts in face or neck. The initial lesion appears to be a lymphangiectasis of the limb, but the subsequent secondary changes arising from lymph stagnation are similar to those occurring in other varieties, and papillomatous excrescences, which may recur even on grafted skin, tend to reach luxuriant development.

**2. Lymphœdema Præcox.**—This characteristic condition, so designated by Allen, Barker, and Hines (1946) on account of its usual onset in the second and third decades, was the commonest type in this series. It occurs predominantly in females (87 per cent in the series described by Allen and others), and usually affects one lower limb. The condition may, however, become bilateral, and rarely the upper limb is involved as well, as in one case in this present review, suggesting a generalized basis for the disease rather than a local infective or traumatic aetiology. The lower abdomen and external genitalia are sometimes involved. The onset occurs without known cause, with painless swelling commencing usually at the ankle, but occasionally elsewhere in the limb. There follows a simple slow enlargement of the whole extremity, with perhaps temporary remissions in the earliest stages. Pain is usually absent, and ulceration rare, although vesiculation with discharge of lymph through small sinuses may occur. The main complaint is of the prodigious size of the limb, which may reach elephantine proportions, precluding normal activities by mere weight; alterations in dress may be necessary both for accommodation and camouflage. When the œdema involves the external genitalia, obvious additional difficulties arise. Secondary inflammatory attacks with cellulitis are infrequent. The disease is slowly and uneventfully progressive, and no spontaneous improvement can be expected in established cases.

Eighteen patients (16 female and 2 male) in this series fell into this group. Two described the onset of the condition as immediately following a minor bruise; and in a third patient it followed an ankle sprain, the swelling failing to resolve; none of these cases gave a history suggesting infection or lymphangitis—only 2 patients have at any time suffered inflammatory attacks.

**3. Infective Lymphœdema.**—Filarial infection requires no description here. In the non-specific group, progression is aggravated by a series of inflammatory episodes often associated with severe constitutional disturbance. The attacks may be ushered in with a high pyrexia, rigors, headache, and vomiting. Commonly a localized erythematous zone is visible on the skin of the affected limb, and, as this extends with ill-defined margin, an underlying diffuse brawny cellulitis makes its appearance; the overlying skin is hot, and its colour varies from pink to heliotrope. The attack subsides within ten days unless it can be aborted in the earlier stages by antibiotics, and leaves the limb more tense and œdematous than before. The later stages of this condition have been designated 'elephantiasis nostras streptogenes', and it has been suggested that recurrent streptococcal invasions produce irreversible changes in the lymphatic trunks and glands and are a direct cause of the disease. In well-marked cases the progression by a series of inflammatory crises is in striking contrast to the quiet uneventful progress of the præcox case, but all lymphœdematous limbs carry some increased liability to infection. Recognition of this group is convenient for the purposes of clinical classification, but there seems some doubt as to whether 'elephantiasis nostras streptogenes' merits consideration as a pathological entity, or whether the recurrent infections merely play an aggravating role in an underlying lymphatic disorder. Trichophytosis, not uncommon in these patients, has similarly been incriminated as an aetiological agent, either directly or as a portal of entry for infection.

FIG. 47.—Congenital lymphœdema.

**4. Secondary Obstruction** in relation to malignancy occurs most commonly in the upper limb as a complication of breast carcinoma, or it may occur after radical mastectomy with axillary clearance, especially when followed by irradiation; in these latter patients the œdema may arise after an interval of months or years, and is not necessarily associated with recurrence of the malignancy. In this connexion it is interesting to note the small incidence of chronic lymphœdema of the leg following radical clearances of the groin glands; post-operative œdema may be slight, transient, or non-existent following extensive removal of inguinal and external

iliac glands. Way (1948) reported lymphœdema which cleared up within eighteen months in cases of carcinoma of the vulva treated by radical excision of vulva, regional glands, and inguinal skin *en bloc*, but without complete primary wound closure.

**5. Trauma.**—These patients usually present a lymphœdema of the distal portion of the limb, following accidents with extensive circumferential stripping of the skin and subcutaneous tissue, or similar destruction from burns, usually aggravated by constrictive scarring. The results of adequate skin replacement are good.

FIG. 48.—Bilateral lymphœdema præcox in a 40-year-old woman; silk threads had been introduced into the right leg and thigh twenty years previously.

**6. Reflux Chylous Lymphœdema.**—These interesting cases are associated with lymphatic obstruction either of the thoracic duct itself, or at the root of the mesenteries where lymphatic trunks from lower limb and intestines both converge upon the cisterna chyli. There is backflow of intestinal chyle into the leg, the subcutaneous zone of which is filled with milky fluid, contrasting with the clear œdema fluid more commonly encountered; the deeper tissues are of normal appearance. Servelle and Deysson (1949) have recorded 5 cases. There was one such case in the present series with associated chyluria and chylous metrorrhœa. After ingestion of Sudan III with a fatty meal, the dye was found in lymph collected from dilated channels in the thigh. The aetiology of the obstruction was obscure.

## DIAGNOSIS

Diagnosis of the well-established case from other types of œdema is usually easy as the appearance and history are characteristic. The massive enlargement of the limb, the thickened skin with normal circulation, the prominent hair follicles giving a 'pig-skin' appearance, the presence of deep furrows at knee and ankle reminiscent of infantile flexion creases, present an appearance unlike other conditions.

Differentiation from the œdema of chronic venous insufficiency is not difficult in advanced cases, the hypertrophic skin of the lymphœdematous limb contrasting with the shiny, atrophic, and often pigmented skin of venous inadequacy. Ulceration is rare in the former and common in the latter. The œdema is firmer in lymphœdema and in the later stages may not pit on pressure owing to secondary changes in the tissue. Warty papillomata are common in lymphœdema, contrasting with the eczematous skin changes of venous insufficiency. Dilated cutaneous venules are seldom visible in lymphœdema. However, in the earlier stages distinction is more difficult; the manner of onset, rapidity of progress, and appearance of the limb aid diagnosis, and phlebography may be of assistance in difficult cases. The two conditions may of course coexist. The majority of patients in the present series were investigated by phlebography, with negative results.

Diseases of a general systemic nature which give rise to œdema require consideration when the condition is bilateral, and such cases should be fully investigated. All cases require thorough abdominal and pelvic examination to exclude neoplasm.

Lipodystrophy involving the lower limbs presents a similar gross appearance, but is of bilateral distribution, usually associated with pelvic obesity, and sometimes with wasting of the upper part of the body. Attacks of cellulitis do not occur as in lymphœdema. The fat is lumpy and often tender on palpation. Relief with elevation is very slight. A lymphœdematous element may be introduced by extensive operations for removal of fat.

## TREATMENT

The numerous surgical procedures described may be briefly classified into four groups.

**1. Attempted Reconstruction of Lymphatic Channels.—**

*a.* By introduction of silk threads (Handley, 1908) or a buried rubber tube (Walther, 1919), and other similar procedures. In one case in the series under review silk threads buried twenty years previously without relief were removed in the form of heavily calcified and rigid rods, obviously without capability of capillary action (*Fig.* 48).

*b.* By transplantation of a living 'lymphatic bridge', consisting of skin, fat, and correctly orientated lymphatics, to by-pass inguinal or axillary obstruction (Gillies and Fraser, 1935; McIndoe, 1935; Mowlem 1948). Few late results have been published, and the procedure probably usually fails in its object owing to irreversible changes in the collecting tree distal to the bridging flap; it is also possible that anastomosis of lymph-trunks by a network of sprouting capillaries at the site of implantation may be inadequate. The procedure is occasionally useful to provide drainage from a localized area difficult to reduce by other means. It was used with moderate success in one case of lymphœdema præcox of the arm in the present series; the forearm had been successfully dealt with by other methods, a persistent œdematous collection around the neurovascular bundle in the upper arm was drained into the supraclavicular zone by a

transplanted skin pedicle. Transplanted flap operations for lymphœdema were reputed to have a high operative mortality, but this is almost certainly no longer true under modern conditions. The procedure represents a rational approach to the problem, and its further development may yet provide a radical cure for the disease.

**2. Attempted Drainage of the Stagnant Subcutaneous Pool into the Muscular Compartments of the Limb (Kondoléon, 1912), or into Bone (Lanz, 1911).**—Such procedures assume patency of the deep channels (which is doubtful) and depend also on adequate anastomosis between superficial and deep systems, taking no account of the regenerative capacity of the deep fascia. The Kondoléon procedure involved the cutting of strips of deep fascia through lateral incisions carried the length of the limb, one end of the strip being thrust into the intramuscular planes, allowing the skin to fall into contact with muscle; this proved the basis of subsequent modifications (Sistrunk, 1918; Homans, 1936). The end-results of 55 modified Kondoléon operations have been reviewed by Ghormley and Overton (1934).

**3. Resection of the Skin and Subcutaneous Tissues, and Grafting of the Raw Surface.**—Most workers have given up attempts at radical cure in favour of palliative measures involving excision of the lymph-sodden tissues. Excision and grafting (in crude form) in filarial cases was reported by Havelock Charles in 1912. Since then procedures involving excision and grafting have been described by a number of surgeons (Macey, 1948; Mowlem, 1948; Pratt and Wright, 1941).

Since 1947 a personal series of cases has been treated at the Queen Victoria Hospital by a procedure designed to re-cover the limb with its existing skin returned in the form of a Wolfe graft, after excision of underlying subcutaneous tissue and deep fascia (Watson 1949). This operation, which is an extension of Homans' method and similar to the procedure carried out by Pratt, was adopted to avoid the extensive flaying of the patient required to obtain sufficient split skin to cover the limb; it was also felt that grafted split skin might be less durable than full-thickness skin. The technique is described below.

**4. Sympathectomy.**—This has no influence on the course of the disease, as reported by Telford and Simmonds (1938).

## SELECTION OF CASES FOR TREATMENT

Traumatic cases with localized distal œdema require appropriate tissue replacement, and malignant cases can be excluded. The management of the remainder falls under three headings :—

**1. The Mild Early Case.**—All such cases should be treated by conservative methods; the extensive surgical measures required have at present nothing to offer the young patient with mild lymphœdema. Mild cases should, however, be treated, and treated *early*. By preventing the collection of œdema fluid, secondary soft-tissue changes may be avoided, and although no cure be obtained, the disease may remain in its mildest form. The problem is largely one of providing adequate external support, thus raising the tissue pressure to the maximum level possible without interfering with the blood-supply. Ordinary elastic stockings are almost useless for this purpose, and a stronger material is necessary. Martin's perforated latex 3 in. bandages (25 gauge) are preferable, applied from the base of the toes to the knee or mid-thigh over a lisle stocking or layer of stockinette. The bandage is applied by the patient

FIG. 49.—Lymphœdema præcox of fifteen years' duration in a woman of 30 years: (A) before, and (B) eighteen months after operation.

on rising in the morning, and re-applied at midday after an hour's rest (if possible) with the limb elevated. Elastic stockings are reserved for special social occasions only. Firm lace-up shoes control the dorsal swelling of the foot. The foot of the bed is blocked at night. A sedentary occupation is preferable.

**2. The Established Case with Secondary Changes.**—Here full recovery of normal dimensions is not obtained with rest and compression. Fifteen such limbs (3 arm, 12 leg) have been treated by radical excision of subcutaneous tissues and deep fascia, with return of the skin as a Wolfe graft; 6 of these limbs had previously been treated by the Kondoléon method. There have now been opportunities to observe these cases for periods of up to four years and the results so far as limb size is concerned have been favourable (*Fig.* 49). The technique is as follows :—

A preliminary period of rest in bed with the limb elevated and compression applied is desirable for 7–14 days. The operation on the leg is carried out with a well-padded Esmarch bandage as a tourniquet around the thigh; pneumatic tourniquets have so far been found unsuitable owing to the high pressure required. The clearance is carried out in two stages, dealing separately with the lateral and medial halves of the limb from knee to toes. The incisions are midlateral, and curve behind the malleoli to the bases of the first and fifth toes respectively. Anterior and posterior dermo-epidermal skin-flaps are raised for

half the circumference of the limb, all fat being meticulously removed from the skin; the flaps which retain some vascularity must be handled with great care. When the medial plane is reached the exposed subcutaneous tissue is totally excised. The cutaneous nerves are sacrificed, but the posterior tibial nerve should not be damaged and care taken in the region of the fibular neck. The scarred and thickened deep fascia is then resected; a plane of cleavage exists between it and the fine gliding layer of areolar tissue and paratenon which covers the muscle bellies and tendons. In the upper third of the leg muscle-fibres arise from the deep fascia, and it is wiser here to thin the fascia than excise it with the possibility of adhesion between raw muscle and skin. The clearance is continued over the dorsum of the foot, the tendon retinacula being carefully preserved. The tourniquet is then released and particular care taken over hæmostasis; the flaps will survive over several ounces of lymph, but will suffer local necrosis over a teaspoonful of blood. Multiple perforations are made in the skin to allow escape of lymph; the skin edges are trimmed to provide normal tension, and suture without drainage is carried out. The limb is dressed with a layer of tulle gras, gauze moistened with saline, and copious wool. The upper extremity of the incision is held open during bandaging from the foot upwards to allow expression of any blood which may have collected during suture. The crêpe bandages must be firmly applied. A plaster back-slab is applied over the bandages to provide immobilization and prevent foot-drop. The first dressing is carried out in seven days. The remaining side of the limb can be cleared as soon as the first is soundly healed.

In the majority of cases operation confined to the zone below the knee provides adequate relief, since this is the part of the limb where secondary changes are most marked and where the effects of increased weight are chiefly felt. In gross distension of the thigh a simple thinning procedure has in the present series been found sufficient. To deal with the whole limb from groin to toes at one sitting is undesirable, as it adds considerably to the time taken over an operation which is already time-consuming and of considerable magnitude; a very extensive one-stage operation would carry a greater liability to surgical shock, and increases the risk of loss of skin. The more limited procedure described may appear cautious, but it has the merit of greater safety in respect both of the patient himself and of the survival of his skin.

The technique is similar for the arm. Here there is an obvious danger that swelling of the digits may be aggravated by a proximal operation, but such an effect has not been marked in the three cases concerned, and skin viability is greater than in the lower limb.

*Post-operative Complications.*—Shock has been negligible and no case has given rise to anxiety. Minor sloughing of skin-flaps, usually near the suture line and often attributable to hæmatoma, has been fairly common, but insufficiently extensive to delay healing to a material extent. In 30 operations the area lost justified the application of a small Thiersch graft as a minor procedure on 7 patients, usually carried out with a local anæsthetic, in order to avoid unnecessary scarring and delay in healing. No skin losses occurred in the arm operations. In 2 cases typical inflammatory reactions with constitutional disturbances occurred in the first few days after operation and each patient experienced an intensely irritative urticarial rash (not a penicillin reaction) on the affected thigh and adjacent lower abdomen at the onset; both responded to antibiotics. Ankle equinus is a definite and entirely preventable risk, and unfortunately developed in one patient who acquired high-heeled shoes as soon as discharged from hospital. All patients should be warned to wear low-heeled shoes until normal ankle mobility is regained and the skin has again become supple. In one case late skin breakdown occurred fifteen months after operation as a result of the development of a large skin vesicle along the lateral scar; this burst and left a raw area which required a free graft.

FIG. 50.—Lymphœdema præcox of four years' duration in a 15-year-old boy: (A) before, and (B) ten months after operation.

*Results.*—In all but two cases, in which the excision was incomplete, and one case (*Fig.* 50) in which there was muscle hypertrophy, it has been found possible to reduce the maximum calf circumference to within 1 in. of the normal side, and observation over several years suggests that this improvement will be maintained. Immediately following operation, the limb is of course more slender than its fellow; increase in girth occurs as soon as the patient gets up, as the skin remains thickened and œdematous. There is no evidence of the development of a collateral lymphatic circulation through deeper channels. Swelling of the ankle below the malleoli and around the Achilles tendon cannot be so satisfactorily corrected owing to the anatomy of this region, and this swelling is of course more evident when the rest of the limb has been thinned. Convalescence must be gradual, and support must continue to be worn after operation for an indefinite period. The prospects should be clearly explained to all patients before undergoing

surgical treatment which is extensive and lengthy; they should be in no doubt that the operation is of a palliative and not of a curative nature. Nevertheless a greatly increased freedom has been achieved by the patients in this series; apart from shoe modifications reversion has been made to normal attire, and jobs which had to be given up have been regained.

A B

FIG. 51.—Reflux chylous lymphœdema: (A) before operation; (B) following recent circumferential free grafting of leg and ulcerated dorsum of foot.

**3. The Severe Case with Skin Deterioration or Ulceration.**—In this group the skin is obviously unsuitable for replacement; this applies also where the hypertrophic skin hangs in redundant folds and forms narrow furrows at the joint flexures; in such cases the excision of transverse wedges of skin and similar devices necessary to fit the flaps back on to the limb seriously jeopardize skin viability. These cases are best resurfaced with grafts of split skin after excision of affected skin, subcutaneous tissue, and deep fascia as above. Three cases in this series have been treated in this way, one being a congenital lymphœdema with a chronic suppurative skin infection, where half the leg was free-grafted; a second patient had a chylous lymphœdema with a chronic ulcer on the dorsum of the foot (*Fig.* 51), and the third was a severe præcox case with papillomatous skin changes.

The early results have been very satisfactory so far as limb reduction is concerned, and the cosmetic appearance not as poor as had been feared. It is too early to assess the capacity of the grafted skin to stand up to prolonged wear and tear whilst nourished by tissue fluid of abnormal constitution.

It is hoped that in the future a procedure will be found to cure this disabling and distressing condition. Such a procedure will no doubt be based on a more accurate knowledge of the factors concerned in the causation and maintenance of the lymph stasis than is yet available. At the present time it is felt that in spite of the severe measures involved, palliative treatment in selected cases is fully justified.

## SUMMARY

1. Certain features of the anatomy and physiology of lymphatic drainage are reviewed in relation to lymphœdema.

2. A clinical classification is given and the diagnosis discussed.

3. The selection of cases for different methods of treatment is considered.

4. The surgical methods employed in the treatment of 18 lymphœdematous limbs are reviewed, and the degree of improvement assessed.

I am deeply indebted to Sir Archibald McIndoe both for his encouragement and for referring many of these patients to me for treatment; also to my other colleagues at the Queen Victoria Hospital in this respect; and to Dr. B. Evans for pathological investigations. My thanks are also due to Mr. Gordon Clemetson for his photography.

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# THE PERSISTENCE OF FŒTAL STRUCTURES IN PYELONEPHRITIC KIDNEYS

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PYELONEPHRITIS is a disease of great importance in childhood. It is almost invariably a complication of transient bacteræmia by coliform organisms secondary to acute enteritis. The initial renal lesion is capillary bacterial embolism of a varying number of glomeruli. As transient bacteræmia by intestinal micro-organisms is so common, the question arises whether all glomeruli are equally vulnerable to

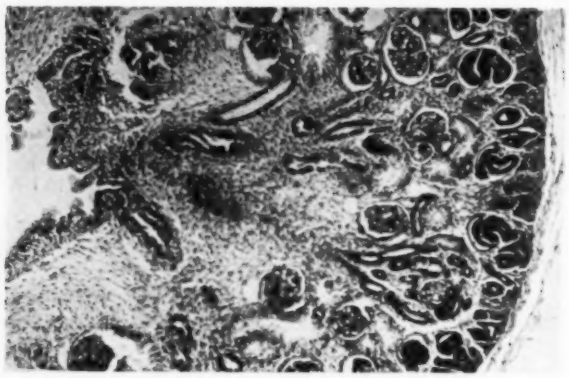

FIG. 52.—Section of the kidney from a 15-week-old fœtus. Note the primitive tubules and glomeruli, the mesenchyme, and the character of the pelvis. The sinusoidal vessels can be seen. H. and E. (× 65.)

capillary embolization, and in this connexion it is pertinent to inquire whether fœtal glomeruli which are found in the kidneys of young children in small numbers are more vulnerable than those which are fully developed. Fœtal glomeruli are always part of a fœtal nephron and such nephrons are usually found in the so-called surface 'scars' which are said to be a feature of chronic pyelonephritis. These are commonly believed to be the end-result of inflammation, but ischæmia resulting from vascular disease or hydronephrosis is thought to play a part in their formation. It is not certain what might be the effect of such disease processes on these rudimentary structures. Fœtal nephrons might regress, mature normally or abnormally, or remain unchanged, and it is only in the last case that they can be recognized. They are far more likely to be found in children's kidneys in which disease must have been of short duration. To establish the prevalence and structure of fœtal nephrons they must be demonstrable in kidneys known to be free from disease, and for this reason specimens from the neonatal period are included in this series. It is clear from the examination of such specimens that fœtal nephrons having a specific structure are found in small numbers lying side by side with normal nephrons.

In the fœtal kidney primitive tubules are regularly disposed and run radially to the periphery of the organ where they curl round as they take part in the formation of a glomerulus. They are straight, rather wide, and lined by deeply staining cells and are quite different from mature collecting tubules (*Fig.* 52). Failure in the normal reduction of the fourth to eighth generation of tubules would result in an abnormally shaped minor calix and the medullary surface would be flattened with regular indentation by the tubules. The appearance is not unlike the map of a river which empties through a delta, and for the sake of simplicity the term 'delta-like' is used to describe it (*see Fig.* 74).

The rudimentary glomerulus has a less distinctive appearance and might well be thought to be atrophic. Infantile glomeruli are characterized by a layer of columnar or cuboidal epithelium closely investing the tufts and sometimes lining the capsules; they may persist in the peripheral zone until the end of the second year of life (Gruenwald and Popper, 1940).

In the fœtus the interstitial tissue is abundant and consists of a loose network of cells, sometimes showing a tendency to concentric arrangement around the primitive structures. The vascular supply within the kidney appears to be formed from simple sinusoidal vessels from which arterioles and arteries subsequently develop.

The purpose of this paper is to describe these structures in infected kidneys. For the reasons given previously, a series of children's kidneys is presented, but this does not imply that such structures have not been found in adults. The renal histology of 12 cases is described fairly fully since so many reports are lacking in this respect and photomicrographs have a limited value. The first 4 are examples of developmental error found in the neonatal period and they are included as controls.

No special methods were employed, but in most cases a section was cut from the entire surface of the kidney, which had been divided longitudinally.

## CASE REPORTS

*Case* 1.—Baby L., a male child weighing 8 lb. 8 oz., died of a subdural hæmatoma within 24 hours of birth. The heart weighed 47 g.

No organic obstruction was found in the whole of the urinary tract.

The left kidney showed normal lobulation but there were several broad depressions on it; it weighed only 8 g. There was a hydronephrosis with erosion of the tips of the pyramids and the tortuous ureter was dilated to a diameter of 1 cm. Microscopically there were patches of normal cortex between the scars, in which fœtal tissue was recognizable. Primitive tubules could be seen running to the periphery, where they curled around rudimentary glomeruli in many of which the capsule was dilated and contained red cells (*Fig.* 53). The glomeruli were not reduced in number and they were all rudimentary or infantile. A few convoluted tubules could be seen in the inner zones of the scars, but they were lined by small cells with reduced cytoplasm and appeared atrophic. The interstitial tissue was plentiful, and varied from adult fibrous tissue to undifferentiated mesenchyme in which there were foci of hæmopoiesis. This tissue lay in concentric layers around some of the

primitive structures. In the outer zones a rich capillary network could be seen. Primitive tubules were present in the medulla (*Fig.* 54), and there were also loops of Henle; they were widely separated by cellular connective tissue.

The right kidney weighed 36 g. and was the seat of an enormous hydronephrosis around which the renal tissue was stretched; there was a large cyst in the cortex. The ureter resembled that on the left. Microscopically there was more normal parenchyma than on the other side, but substantial areas of fœtal tissue were present

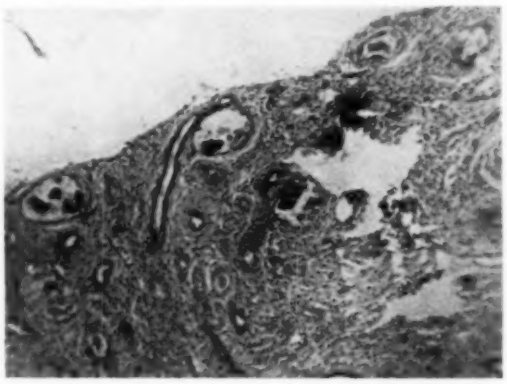

FIG. 53.—*Case* 1. Left kidney. Cortex showing primitive tubule looping around rudimentary glomerular tuft lying in a dilated capsule. H. and E. (× 55.)

(*Fig.* 55). In the cortico-medullary zone some of the tubules were small and had no lumen; they are regarded as rudimentary (*Fig.* 56).

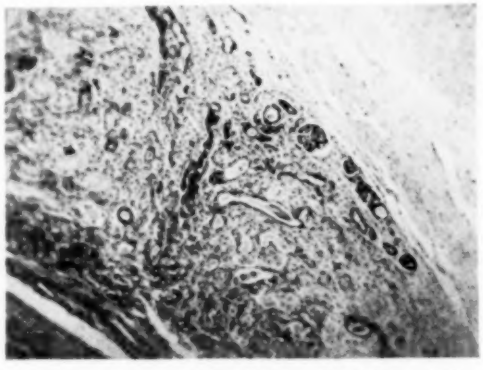

FIG. 55.—*Case* 1. Right kidney. Primitive tubules in cortex showing characteristic form and course. Note the cellular undifferentiated interstitial tissue. H. and E. (× 55.)

There was no cellular infiltration in either kidney and no lymphoid follicles were found. The arteries and arterioles were normal.

**Comment.**—The normal birth weight and the presence of normal renal cortex prove that this is not a case of prematurity and it may be assumed there was neither vascular disease nor infection. There was more normal parenchyma on the side where the hydronephrosis was larger, which suggests that the lesions are not the result of pressure from it. The hydronephroses and hydro-ureters without any obstruction may be regarded as evidence of maldevelopment.

In view of the weight of an otherwise normal heart, it is considered that this is a case of antenatal hypertension. (Parrot, Joseph, and Nesbit, 1951.)

*Case* 2.—A female baby, one month premature, weighed 3 lb. 12 oz. and died on the second day after birth from a subdural hæmorrhage. The mother had a feverish illness during the second month of this, her fifth pregnancy, and during the sixth month a pain in her right side was considered to be due to cholecystitis. Her other children are all alive and well except one who died of jaundice in infancy.

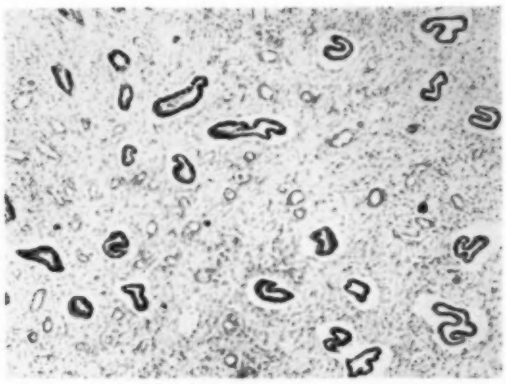

FIG. 54.—*Case* 1. Left kidney. Medulla showing primitive tubules. Some are branching. Normal collecting tubules and Henle's loops may also be seen. H. and E. (× 55.)

At post-mortem the heart was found to weigh 15 g. and was normal apart from blood-cysts on the aortic valve. Both kidneys were double, with double ureters.

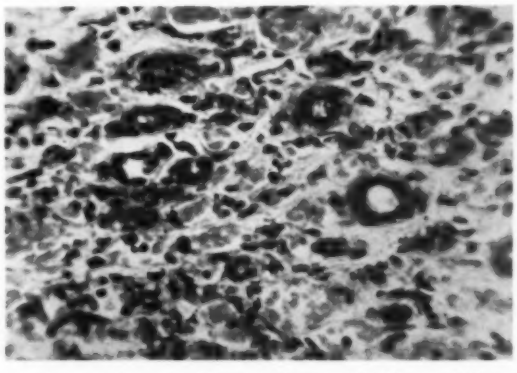

FIG. 56.—*Case* 1. Right kidney. Primitive tubules in cortico-medullary region. Note occasional solid cords of the characteristic cells. H. and E. (× 115.)

The upper kidneys consisted of multiple cysts but the lower ones were normal apart from malrotation, and there were scars on the surface of the right one. Three ureters were normal but the fourth (which was the upper one on the right) was dilated and tortuous. No hydronephrosis or hydrocalix was found in the lower kidneys, the structure of which is described below.

Microscopically there was generalized failure of full development except in the medulla, where only small areas were abnormal. The appearance of the cortex is seen in *Fig.* 57, and the primitive tubules and glomeruli are well shown. In the cortico-medullary zone many of the primitive tubules were cord-like and in the medulla they vary in size (*Fig.* 58). The interstitial tissue was inconspicuous in the cortex, but was more abundant in parts of the medulla, where it resembled mesenchyme and in places formed concentric rings around the primitive

tubules. One or two foci of hæmopoiesis were present, and there was a capillary network in parts of the cortex; the other vessels were normal. There was no cellular infiltration and no lymphoid follicles were found. Parts of the pelvic surface showed the delta-like appearance.

Occasional foci of rudimentary renal tissue were present in the cystic upper kidneys.

**Comment.**—This case is included for comparison with older children in whom there is renal infection and with *Case* 1 where there was hydronephrosis. It may be thought that the failure of development in the kidney is simply part of the baby's prematurity; but in the task of assessing this factor, the presence of normal medullary tissue and the congenital anomalies of the urinary tract should not be overlooked.

*Case* 3.—Baby P. This baby died an hour after birth with blue asphyxia; he weighed 6¼ lb. His mother was 39 years old and she had œdema of the feet during pregnancy, but her blood-pressure was normal and she was otherwise well. One previous child had died of gastro-enteritis when 6 months old.

Necropsy revealed two small kidneys, the larger right one measuring 3 × 1·4 × 0·7 cm. The normal markings were absent, but there were discoloured patches on the surface corresponding to greyish-white streaks in the cortex. Neither pelvis was dilated but both ureters were enlarged and tortuous; no obstruction was found in any part of the urinary tract. The baby died of interstitial pulmonary and mediastinal emphysema. The weight of the heart was not recorded.

Only one section of the kidney was available for study and it showed great disturbance of the renal architecture. There were scanty groups of infantile glomeruli and their associated tubules, and between them lay plentiful primitive tubules and rudimentary glomeruli or proglomeruli (*Fig.* 59). The interstitial tissue in the cortex was rather scanty, but in places it could be seen to be undifferentiated and there were numerous foci of hæmopoietic cells among which (but not apart from them) lay a number of lymphocytes. There were numerous islands of fœtal cartilage in the cortex. The medulla consisted of scanty primitive tubules lying in an abundant cellular mesenchyme (*Fig.* 60). Its pelvic surface was normal.

The whole of the cortex was permeated by a capillary network, but the arteries and arterioles were normal.

**Comment.**—This case is included to illustrate primitive structures. There was no hydronephrosis, no vascular disease, and no infection. Although cellular infiltrates were present they were associated with hæmopoiesis. This baby was not premature and the renal histology is quite outside the limits of normal.

FIG. 57.—*Case* 2. Right kidney, showing primitive tubules and glomeruli in cortex. H. and E. (× 55.)

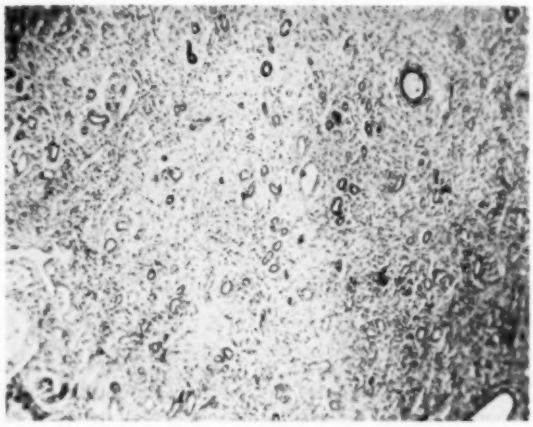

FIG. 58.—*Case* 2. Right kidney, showing primitive tubules and concentric arrangement of interstitial tissue in medulla. H. and E. (× 55.)

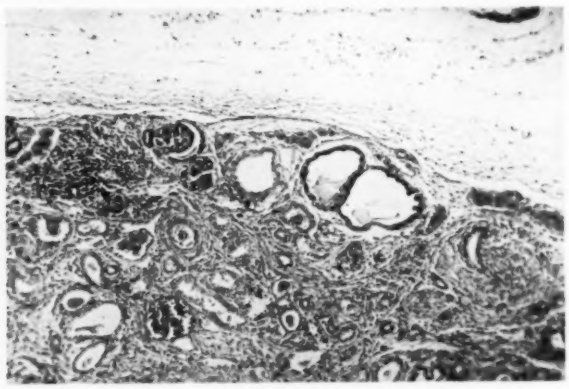

FIG. 59.—*Case* 3. Primitive tubules and glomeruli. Note the proglomerulus, somewhat out of focus on the right. The cavernous capillary network is not well shown in this area. H. and E. (× 55.)

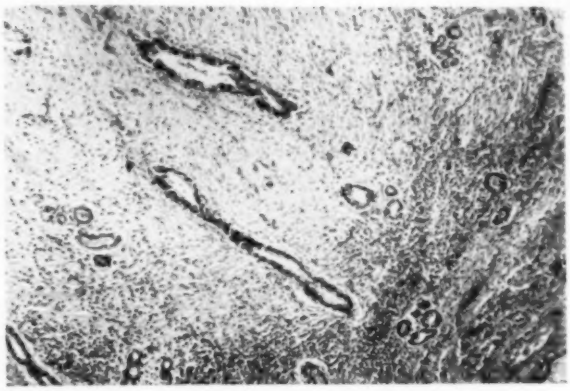

FIG. 60.—*Case* 3. Primitive structures in the medulla. Note the smaller tubules in the cortico-medullary zone and the normal collecting tubules on the left. H. and E. (× 55.)

*Case* 4.—John L., aged 3 weeks. This baby failed to thrive from birth and he died of intracranial hæmorrhage following thrombosis of the cerebral sinuses. The birth weight is not recorded, but he was not considered to be premature. Post-mortem examination revealed asymmetry of the skull and mandible and the testes were still in the pelvis. The left kidney was described as hypoplastic and there was a bilateral hydronephrosis with normal ureters and bladder.

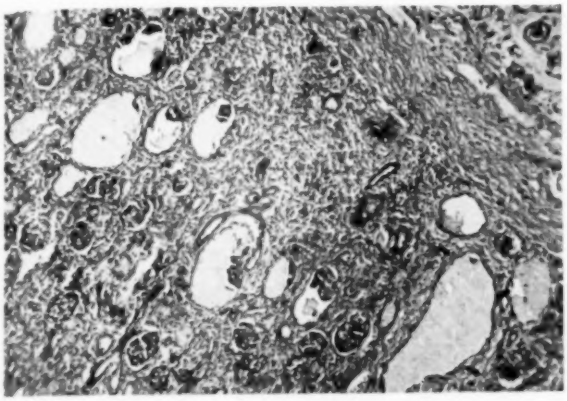

FIG. 61.—*Case* 4. Left kidney. Cortex showing centrally a primitive tubule looping round a rudimentary glomerulus. Note the dilated capsules. H. and E. (× 55.)

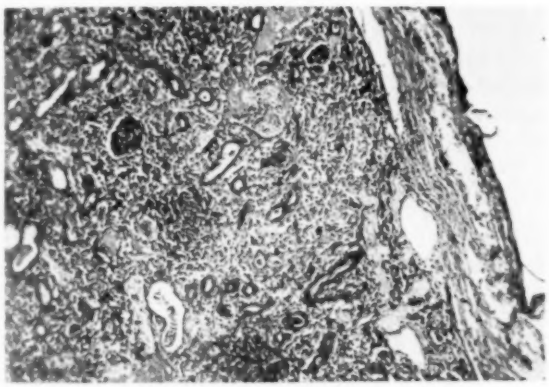

FIG. 63.—*Case* 5. Cortex showing primitive tubules lying in an area of acute inflammation. Note the capillaries containing coagulated plasma. H. and E. (× 55.)

Microscopically most of the right kidney was normal, but there were several areas in the cortex and medulla where primitive tubules could be seen. A few subcapsular glomeruli were rudimentary and many had dilated capsules resembling those seen in a polycystic kidney; there was a rich network of dilated capillaries around them. The medullary pyramids were normal and the connective tissue was not remarkable; there was no cellular infiltration. Small deposits of calcium could be seen in the perirenal tissues and there were occasional islands of cartilage in the cortex.

The left kidney was much less fully developed and throughout the cortex primitive tubules could be seen running to the subcapsular zone, where they curled around primitive glomeruli (*Fig.* 61). Many of these glomeruli were rudimentary, with dilated capsules, and there were other cysts lying among them. In the outer zone of the cortex the convoluted tubules were very scanty and many seemed to be atrophic. The medullary pyramids were not flattened, but many of them contained primitive tubules and undifferentiated mesenchymal stroma (*Fig.* 62). There was a capillary network in the outer cortical zone and the interstitial tissue was plentiful and cellular; there was no cellular infiltration. The larger vessels were normal.

**Comment.**—The presence of cartilage as well as normal cortex in the right kidney supports the view that there was a developmental defect which has a focal distribution. The generalized abnormalities of the left kidney cannot be the result of

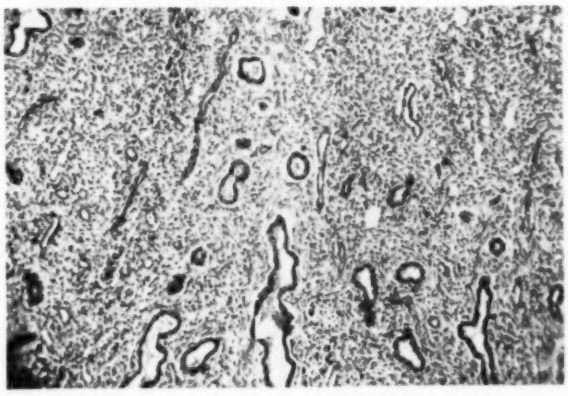

FIG. 62.—*Case* 4. Left kidney. Primitive tubules and connective tissue in medulla. H. and E. (× 55.)

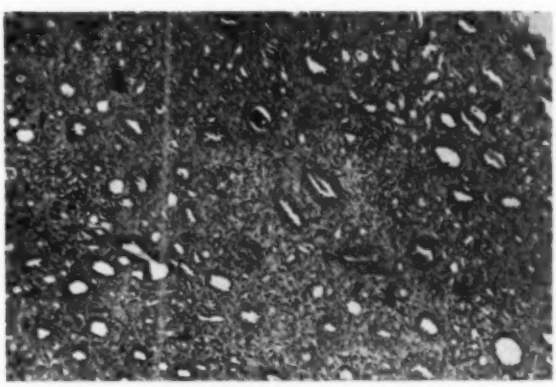

FIG. 64.—*Case* 5. Medulla. H. and E. (× 55.)

prematurity and the marked difference between the two sides suggests that hydronephrosis had not played a major role. There was no evidence of infection or vascular disease.

*Case* 5.—Heather A., aged 7 months, had a history of recurrent abdominal pain, pyrexia, and infected urine since she was three months old. She was found to have a bifid ureter and the left kidney was removed. A month before operation, while she had pneumonia, her blood-pressure was 100/55 mm. Hg; the normal for this age is stated to be 80 mm. systolic (Fishberg, 1939) and less than 85/50 (Nash, 1951).

Half the kidney was received. The upper part of the bifid ureter was grossly dilated and tortuous but the lower was thick-walled and only slightly enlarged. The kidney was double and the upper part grossly hydronephrotic; the lower half showed only slight pelvic dilatation. The surface was nodular and there were many irregular depressed scars.

Microscopically the lower part consisted of normal cortex separated by the scars where there was acute inflammation with abscess formation. The outer glomeruli were, of course, infantile in type and many

of the tufts were small, with dilated capsules. No fibrotic tufts were found, and in only a few glomeruli was there any evidence of pericapsular fibrosis. Some of Bowman's capsules were lined by columnar epithelium, but there were neither adhesions to the tuft nor crescent formation. Most of the very scanty tubules resembled collecting tubules, but some were more densely stained and curled or branched just under the renal capsule; these were thought to be primitive in type (*Fig.* 63). Some contained pus and others a little albuminous material. The interstitial tissue was abundant, œdematous, and heavily infiltrated by polymorphs, lymphocytes, and plasma-cells. In the medulla, which was not greatly abnormal, there were areas where the tubules were reduced in number and many were lined by tall columnar cells. Here the interstitial tissue was œdematous and it was only lightly infiltrated by inflammatory cells. The large arteries and the arterioles appeared normal, but there was a well-marked capillary network under the capsule. (*Fig.* 64.)

It should be made quite clear that the normal cortex between the scars was free of any sign of inflammation or other abnormality.

**Comment.**—This case of acute suppurative pyelonephritis is included because there are gross developmental errors associated with microscopical features suggesting persistent fœtal tissue. Either the structures in the outer cortex were the result of infection or the very slight hydronephrosis, or they were due to maldevelopment. It might be suggested that metaplasia had occurred in the tubules, but an appearance such as that shown in *Fig.* 63 is highly suggestive of a primitive type, especially when compared with those seen in the other cases.

*Case* 6.—Angela G., aged 2 years, was a healthy child until she was admitted to hospital with bronchopneumonia and she then developed a renal infection which was cured by the use of sulphonamides. A retrograde pyelogram showed malrotation of the left kidney and clubbed calices, but it was remarked that the degree of enlargement of the pelvis was minimal. Her blood-pressure was 100/75 mm. Hg, and the normal is given as less than 92/58 and 85/50, by Fishberg (1939) and Nash (1951) respectively.

The left kidney weighed 35 g. and 4 cm. of normal ureter was attached to it. The surface showed normal lobulation and a few tiny scars; no cortical artery was found. The calices were dilated and lined by thick walls and the pelvis was moderately enlarged, with a narrow pelvi-ureteral junction.

Microscopically much of the kidney was normal, but there were areas of abnormal cortex where numerous primitive tubules could be seen running to the periphery and curling around under the capsule, some being related to glomeruli (*Fig.* 65). In the same areas other more developed tubules could be seen, but they were scanty and some appeared atrophied. Although some of the primitive tubules were somewhat dilated, this was not a marked feature. The glomeruli in the normal cortex had all lost their infantile epithelium, but it was retained in many of those lying in the scars. Some of the glomerular tufts were rudimentary and were undergoing fibrosis, and groups of fibrotic glomeruli could be seen; some of them lay in direct association with a primitive tubule. The interstitial tissue was plentiful, but its true structure was difficult to make out because it was infiltrated by lymphocytes and a few plasma-cells. True lymphoid follicles were present near the hilar structures, and lymphoid aggregations without germinal centres were plentiful in the subcapsular zone of the scars. Both the large arteries and the arterioles were thick-walled, but neither showed any intimal thickening; there was no excess of capillaries in the scars.

In the medulla there were numerous primitive tubules lying in cellular connective tissue which resembled mesenchyme, but there were also normal structures. It showed a mild cellular infiltration which included a number of leucocytes. The pelvic surface was covered by a fairly thick layer of epithelium and the orifices of the large tubules in it gave a delta-like appearance.

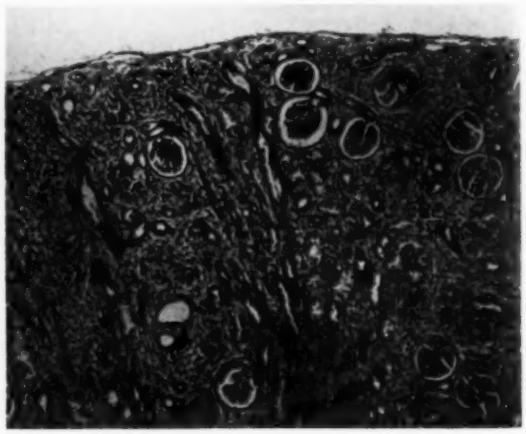

FIG. 65.—*Case* 6. Cortex showing primitive tubules. Note sclerosis of some of the glomeruli, especially in right lower quadrant where a sclerotic tuft lies in contact with a primitive tubule. H. and E. (× 55.)

**Comment.**—Although this kidney had been infected for only a short time, a number of fibrotic glomeruli were seen and the question arises whether their appearances can be due to the infection.

There can be little doubt about the nature of the fœtal tissue in the scars. It is instructive to note that the usual capillary network in the outer cortex was absent, confirming that it is not related to infection as might be suggested by some of the previous cases. The hydronephrosis was minimal and mainly affected the calices, yet the delta-like appearance of the medullary surface was well marked. This is consistent with the suggestion of an error in the reduction of the early generations of primitive tubules.

*Case* 7.—Margaret W., aged 3 years 8 months. She suffered from malignant hypertension (having a blood-pressure of 260/220 mm. Hg) and nephrectomy was undertaken because two partly calcified arterial aneurysms were found in the hilum of the right kidney. Her urine was never infected while she was under observation and the surgeon considers she never had pyelonephritis.

The kidney weighed 20 g. and much of it appeared normal. Several large irregular depressed scars occupied one half, which was consequently the smaller. There was no hydronephrosis or hydrocalix and the ureter was normal. Both aneurysms were partly occupied by organized thrombus and there could be no doubt that the normal part of the kidney was supplied by one of the vessels so involved.

Histologically it is difficult in a brief description to do justice to the great variability of the renal parenchyma. One half of the organ was normal and a patch of the opposite pole, which appeared normal macroscopically, was composed of the so-called thyroid-like tissue (Weiss and Parker, 1939). The 'scars' lay between these two, and there was little recognizable renal tissue in them. Both the cortex and medulla were formed of undifferentiated cells, but a few rudimentary structures could be

seen in them. In the cortex there were tiny primitive tubules, some without a lumen, and occasional rounded structures resembling proglomeruli as well as a few rudimentary glomerular tufts (*Figs.* 66, 67). In one scar there were numerous fibrotic tufts lying in the mesenchyme without any capsules; while they might be degenerate, they might equally well be rudimentary

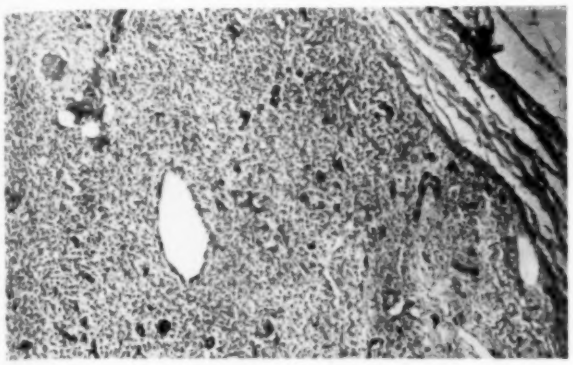

FIG. 66.—*Case* 7. Primitive tubules lying in undifferentiated tissue in the cortex. H. and E. (× 55.)

structures in which vascularization has failed. The only tubules in these areas were tiny and primitive and were seen in both medulla and cortex (*Fig.* 68). There was a moderate capillary plexus and the interlobular arteries, which ran straight to the depressed surface, were thick walled. They showed no evidence at all of thrombosis or embolism, and their walls, which contained no collagen (Bell, 1950), were formed from large cells which appeared somewhat undifferentiated. There was a fairly abrupt change to normal cortex at the edges of the scars, but the narrow intermediate zone contained a number of fibrotic and infantile glomeruli as well as others undergoing pericapsular fibrosis. There was no fibrosis and no cellular reaction here or in any other part of a section of the entire cut surface.

The aneurysms resembled those described in the cerebral arteries by Carmichael (1950) and their medial coat appeared to be incomplete; the intima was covered by thick layers of organized thrombus. The remainder of the vessels showed a slight patchy intimal thickening, so slight that it would be difficult to imagine any impediment to the flow of blood.

**Comment.**—I believe these scars to be composed of undifferentiated metanephric tissue. If they were secondary to the vascular disease the local replacement of almost all the renal parenchyma by richly cellular tissue would be inexplicable; there is no fibrosis and neither vascular nor cellular reaction around their edges. Hydronephrosis cannot be a factor since there was none. Clinically there was nothing to suggest past or present infection and there was no cellular infiltration. Weiss and Parker (1939) consider the thyroid-like areas of tubular dilatation to be diagnostic of pyelonephritis, but Bell (1950) remarks that they are not confined to this disease. In addition the scars in this kidney are totally different from those described by Weiss and Parker (1939). The cellular tissue is not unlike that seen in some types of Wilms' tumour (Allen, 1952), but there is no tumour and nothing to suggest either neoplasia or hyperplasia. It is partly on this resemblance that I regard the tissue as metanephric.

The fibrotic glomerular tufts lying in the 'scars' are worth noting, and also the fact that one of the arteries in which there was an aneurysm containing thrombus supplied the normal part of the kidney.

*Case* 8.—Michael W., aged 5½ years. This child developed hæmaturia and increased frequency of micturition only two months before operation, before which he had always been well. His urine was infected, and clinical

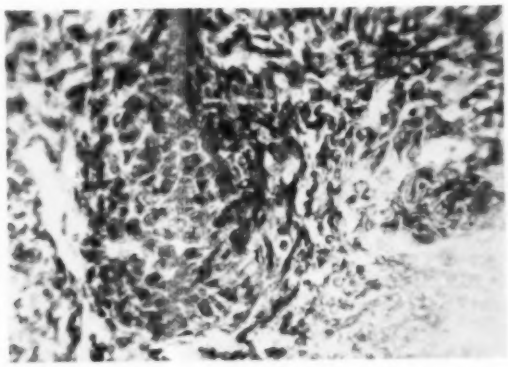

FIG. 67.—*Case* 7. A proglomerulus in the undifferentiated tissue with another smaller one beside it. H. and E. (× 125.)

investigation showed a hydronephrosis and hydro-ureter but no organic obstruction. His blood-pressure was 115/85 mm. Hg, and at this age Fishberg (1939) regards 94/65 mm. as normal, while Nash (1951) gives the figure of 70/40 mm.

The left kidney weighed 55 g. and about 30 cm. of thickened dilated ureter was attached to it. On the surface there were numerous nodules separated by depressed areas which were mostly seen at either pole. The cut surface revealed a large hydronephrosis with dilated calices and flattening of the medullary pyramids.

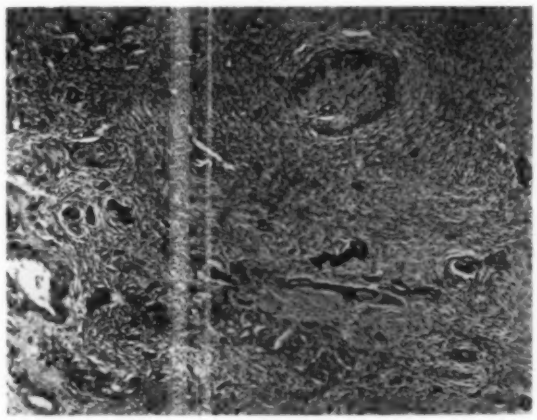

FIG. 68.—*Case* 7. Primitive tubules in the cortico-medulla. The nature of the structure in the upper right quadrant is unknown, but it is thought to be a stage in formation of a thick-walled arteriole. H. and E. (× 65.)

A section of the entire cut surface showed a great deal of normal cortex and medulla. At each pole the width of the cortex was much reduced and there was no trace of any glomeruli at all; the cortex consisted of tubules dilated to a varying extent and containing eosinophilic albuminous material. They were lined by cuboidal epithelium which became taller and more deeply staining in the outer zones until tiny primitive ones were seen under the renal capsule (*Fig.* 69). The interstitial tissue was composed of large oval cells and was more abundant in the cortico-medullary zone, where there was an appearance suggestive of condensation to form primitive tubules

(*Fig.* 70). In parts of the medulla large, branching, somewhat primitive tubules could be seen and the connective tissue was more differentiated. A few small lymphoid follicles could be seen near the pelvis and there was a mild patchy lymphoid infiltration throughout the scarred areas. There were many tortuous thick-walled arterioles running to the surface and between them a well-marked cavernous capillary plexus. The arteries were also thick walled, but there was no intimal change in any of them; one ran radially right up to the capsule.

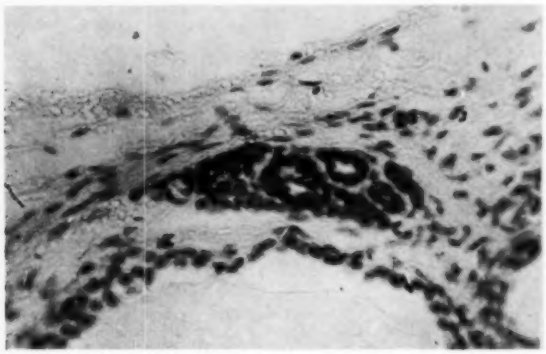

FIG. 69.—*Case* 8. Primitive tubules in scarred cortex. H. and E. (× 125.)

Between the scars the renal parenchyma was quite normal, although there were dilated calices related to it.

**Comment.**—The evidence of congenital anomaly is not so clear in this case, although unilateral hydronephrosis without any obstruction is highly suggestive

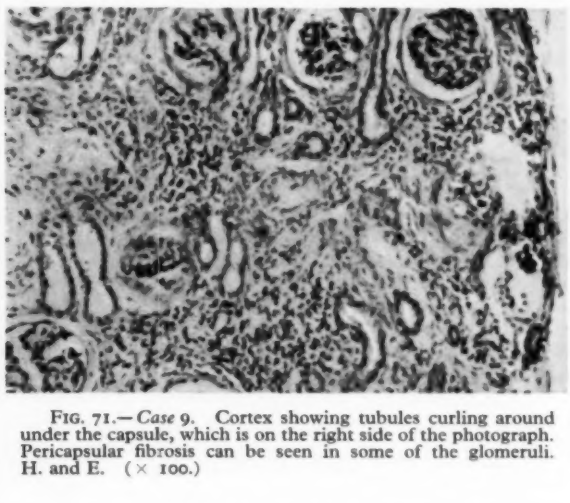

FIG. 71.—*Case* 9. Cortex showing tubules curling around under the capsule, which is on the right side of the photograph. Pericapsular fibrosis can be seen in some of the glomeruli. H. and E. (× 100.)

of it. It is thought that no glomeruli have ever formed in the scars since there are no traces of any degenerated ones. The capillary plexus and primitive tubules are suggestive of a localized developmental defect. The distribution of the lesions at either pole is interesting, since Keibel and Mall (1912) state that each advance in further development of the nephrons first occurs there.

*Case* 9.—Jane R., aged 6 years. This child had a history of recurrent attacks of pain in the right loin, fever, and increased frequency of micturition for two and a half years. Intravenous pyelograms showed no secretion from the right kidney, but there was a calculus in the lower end of the ureter and it was removed. The symptoms recurred and pyelograms showed a hydronephrosis. There is no record of the blood-pressure before nephrectomy, but it was found to be 130/80 mm. Hg afterwards. The normal for this age and sex are given by Fishberg (1939) as 94/63 mm. and by Nash (1951) as 85/50 mm.

The kidney, together with 8 cm. of thickened ureter, weighed 34 g. and it was covered by raised nodules separated by depressed somewhat translucent tissue.

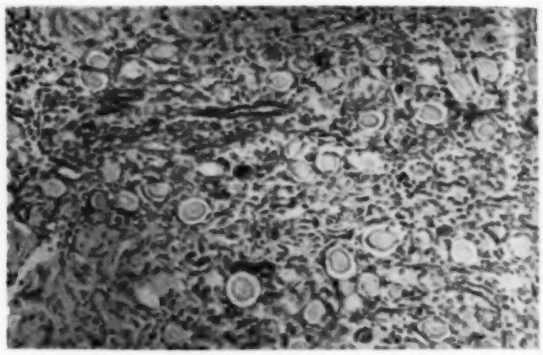

FIG. 70.—*Case* 8. Primitive tubules in the cortico-medullary region. H. and E. (× 75.)

The cut surface revealed a moderate dilatation of a thickened pelvis especially affecting the calices. There was a stump of a cortical artery in the lower pole.

Microscopically the nodules were seen to be normal renal tissue, but the depressions were densely infiltrated by lymphocytes and there were lymphoid follicles in the

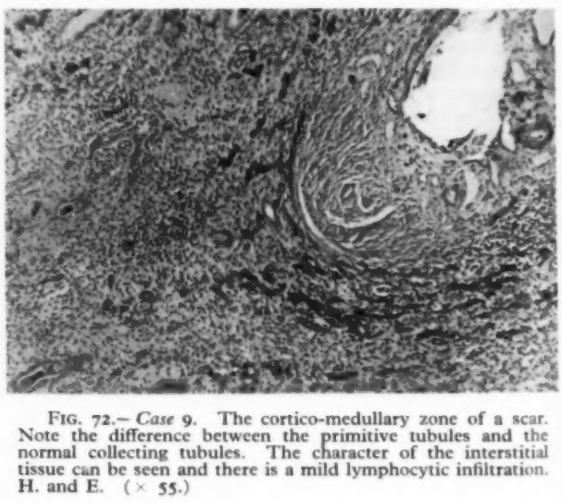

FIG. 72.—*Case* 9. The cortico-medullary zone of a scar. Note the difference between the primitive tubules and the normal collecting tubules. The character of the interstitial tissue can be seen and there is a mild lymphocytic infiltration. H. and E. (× 55.)

cortico-medullary tissue. Although the width of the cortex was much reduced, there was no interstitial fibrosis; indeed much of the plentiful interstitial tissue was composed of large ovoid cells and resembled mesenchyme. There was crowding of the glomeruli and many of them were small fibrous masses or small abnormal tufts with concentric fibrosis of Bowman's capsule; some of these tufts were covered by cuboidal epithelium similar to those seen in infantile glomeruli, and some showed early fibrosis. Tubules were rather scanty and resembled the collecting type, but there were deeper staining ones in the subcapsular region curling round as shown in *Fig.* 71. Many contained albuminous material and others contained pus. In the corresponding parts of the medulla there were very few tubules and some resembled the primitive

type seen in other specimens (*Fig.* 72). The pelvic surface of the pyramids was flattened and covered by a thick layer of epithelium which was continued into the tubules. The arteries and arterioles were thick walled but had a normal intima and there was a capillary network in the peripheral cortex.

**Comment.**—It is difficult in this case of active pyelonephritis to be sure that the histological changes are not due to infection. Nevertheless the tubules curling around in the subcapsular zone, the primitive tubules in the medulla, and the nature of the connective tissue are all suggestive of imperfect development. In addition there is the same cavernous blood-supply and the rudimentary glomeruli already described in the previous cases. It has been suggested above that the fibrotic glomerular remnants (as opposed to pericapsular concentric sclerosis) could follow failure of development just as readily as degeneration.

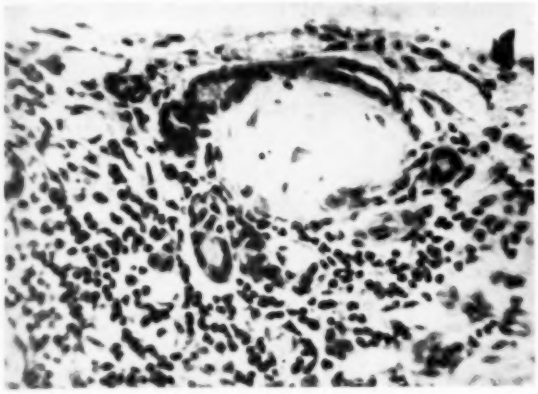

FIG. 73.—*Case* 10. Subcapsular region showing a primitive tubule looping round a fibrotic glomerular tuft. H. and E. (× 125.)

*Case* 10.—Diane N., aged 9 years. Since she was 18 months old this child had a recurrent infection of the urinary tract. Subcutaneous pyelography showed a mild hydronephrosis on the right side with dilatation of the minor calices. Before nephrectomy the blood-pressure was 120/85 mm. Hg, which is considerably higher than the normal values given by Fishberg (1939) as 92/62 mm. and by Nash (1951) as 96/58 mm.

The kidney weighed 50 g. and its surface was nodular. Large irregular depressed scars separated islands of normal cortex. An upper calix was dilated and the ureter was thickened. There were two cortical arteries in the upper pole.

Histologically much of the kidney appeared normal except for microscopic 'scars' and an excessive number of collecting tubules immediately beneath the renal capsule. In the larger depressions the cortex was reduced in width and there was great glomerular crowding; the tubules were very scanty. These glomeruli were almost all small fibrous nodules, but on the edges of the scars there were dilated Bowman's capsules containing apparently atrophic or perhaps rudimentary tufts; some of the capsules were thickened by concentric fibrosis. No infantile glomeruli were found. No normal convoluted tubules were to be seen in the scars, but there were small primitive tubules recognizable in the subcapsular region (*Fig.* 73) and one or two of them contained plasma-cells. The corresponding part of the medulla was grossly abnormal by reason of large branching collecting tubules lined by thickened epithelium which was continued over the flattened pelvic surface (*Fig.* 74). Some of their branches strongly resembled primitive tubules and differed markedly from normal collecting tubules in the same pyramid. The interstitial tissue was richly cellular and appeared to be somewhat undifferentiated and there was a mild infiltration by lymphocytes and a few plasma-cells. In the scarred cortex there was a cavernous vascular network and many arterioles whose muscle coat was greatly thickened ran in a tortuous fashion almost to the renal capsule. Some of the larger arteries seemed to have a slight intimal thickening, but the lumen could hardly be affected by it.

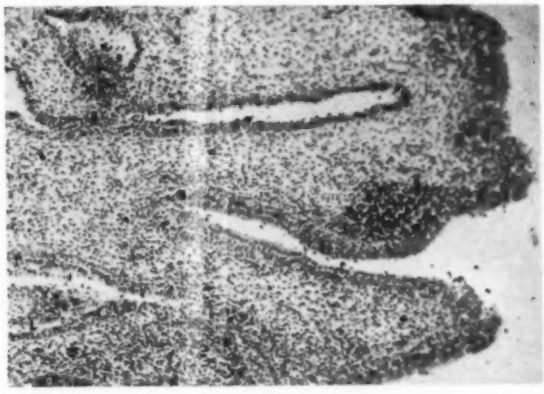

FIG. 74.—*Case* 10. The 'delta-like' appearance of the pelvic surface of the medulla. These tubules are, of course, not considered to be primitive. H. and E. (× 125.)

**Comment.**—The diagnosis of persistent fœtal tissue in this case rests on the presence of primitive tubules in the medulla, cortico-medullary region, and the subcapsular zone. The kidney was infected.

*Case* 11.—Cynthia B., aged 11 years. This child suffered from constant enuresis from birth and was found to have an ectopic ureter which opened into the vestibule just behind and to the left of the urethral orifice. Cystoscopy revealed no cystitis and the ureteric urine contained no leucocytes and was sterile. There is no record of the blood-pressure. The left kidney lay on the bifurcation of the left common iliac artery and it was the size of a small plum. Its ureter entered the lower pole and there was no pelvis.

Two sections were received. Most of the cortex was normal but there were one or two small depressions in which tiny primitive tubules could be seen as they curled around under the renal capsule. One infantile glomerulus was found in a column of Bertini, but almost all the remainder are fully developed and normal. In *Fig.* 75 the cavernous vessels in one of the scars can be seen and they were accompanied by thick-walled arterioles surrounded by concentric layers of fibrous tissue running close to the surface. There was a mild lymphocytic infiltration of the scars.

The medulla was made up of primitive tubules of all sizes lying in a richly cellular, partly fibroblastic connective tissue which ran around them in concentric layers (*Fig.* 76).

The arteries and arterioles showed no intimal thickening.

**Comment.**—It is unusual to see the medulla so much more abnormal than the cortex. The appearances are not likely to be the result of vascular disease nor of infection, since there is no evidence of either. In view of the obvious congenital anomaly it is thought that the tubules seen in the medulla and the cortex are primitive structures.

*Case* 12.—Rosemary H., aged 11 years. This child had been incontinent since she was 2½ years old, with increased frequency and urgency of micturition. She is said to have had endocarditis, but was discharged from the hospital as normal. Before nephrectomy her blood-pressure was 180/130 mm. Hg.

Half the left kidney, cut vertically, was received, and it weighed 3·5 g. The cortex was thin and the surface nodular. The calices were dilated and the medullary pyramids flattened, but the remainder of the pelvis was not dilated and the ureter was normal.

FIG. 75.—*Case* 11. Primitive tubules in relation to a scar and lying in the cortico-medullary zone. Note the thick-walled arterioles close to the surface, and the large capillaries. H. and E. (× 55.)

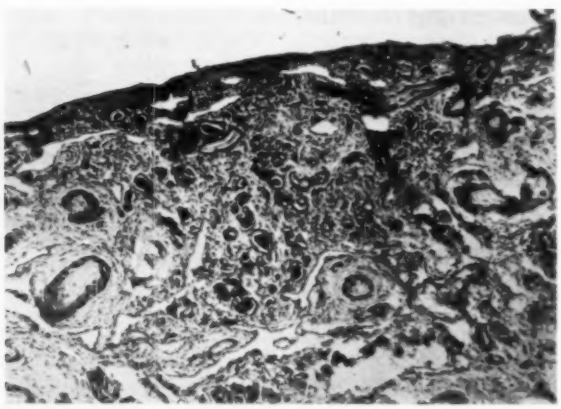

FIG. 77.—*Case* 12. Primitive structures in scarred cortex. Note rich cavernous vascular network. The appearance of blocking of the thick-walled arteries is an artefact and they are filled with coagulated fluid containing red cells. H. and E. (× 75.)

Microscopically the only normal cortex was seen in the columns of Bertini and one small patch under the capsule. Elsewhere there were no glomeruli apart from a few tiny fibrous masses, and the cortex consisted of blood-vessels and tubules. The majority of the vessels were sinusoidal, but there were numerous thick-walled arterioles and arteries running close to the surface and they were surrounded by concentric layers of fibrous tissue. The tubules were small, some appeared dilated, many contained albuminous material and they resembled collecting tubules; no convoluted tubules were seen in these areas. Here and there a few resembled primitive tubules in their position and structure (*Fig.* 77). Much of the medulla seemed to be completely absent, but where it could be found a few primitive tubules were seen and there was early fibrosis (*Fig.* 78). There was a mild patchy lymphocytic infiltration but neither plasma-cells nor cellular casts were found. The classical features of malignant hypertension were present in one or two arterioles, but most of them, although showing both intimal and medial thickening, have a wide lumen and were otherwise normal.

**Comment.**—This kidney has been the seat of long-standing recurrent infection. The similarity of the structures thought to be primitive tubules to

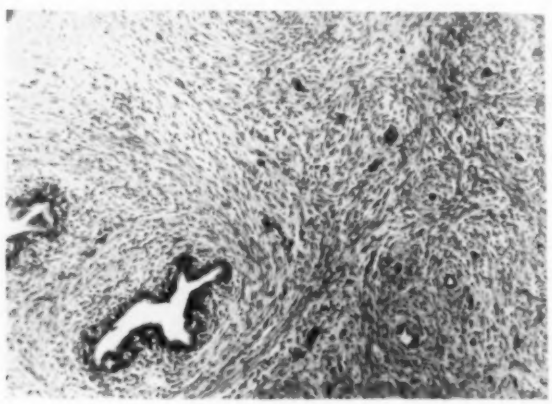

FIG. 76.—*Case* 11. Primitive tubules in the medulla. Note variation in size and concentric whorled arrangement of the primitive connective tissue. Although this photomicrograph does not show enough of the medulla, these larger tubules are very numerous and are not cross-sections of the calices. H. and E. (× 75.)

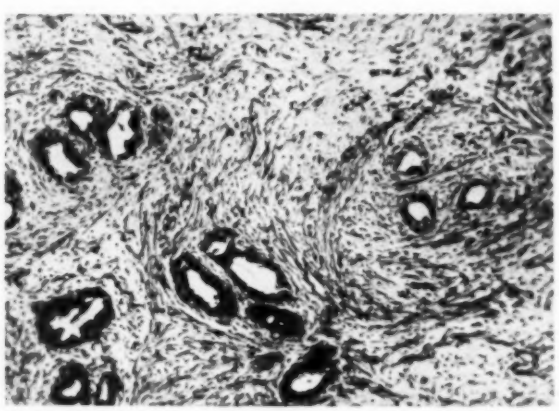

FIG. 78.—*Case* 12. Medulla showing primitive tubules and early fibrosis in whorled connective tissue around them. H. and E. (× 100.)

those seen in non-infected kidneys, and the relative absence of normal structures in the cortex in association with the rich capillary network, suggests a parenchymatous congenital abnormality. From comparison with the previous cases it is doubtful if the vascular changes or the dilated calices could be the cause of the histological appearances.

## DISCUSSION

There is nothing new in the concept of pyelonephritis superimposed on a 'hypoplastic' kidney (Longcope and Winkenwerder, 1933) and recently Emmett, Alvarez-Ierena, and McDonald (1952) have confessed their inability to separate the two conditions on any grounds. Rudimentary structures

have been recognized in association with developmental anomalies of the kidney (*see below*), and it is the purpose of this paper to record them in pyelonephritis. Weiss and Parker (1939) considered the microscopical appearances of infected kidneys to be entirely the result of the inflammation, and even before this, Butler (1937) simply described the structural changes as ' pyelonephritis '. It is therefore to be expected that the structural features described in this paper are usually attributed to infection, hydronephrosis, or ischæmia, and such terms as the ' medulla of pyelonephritis ' are freely used in discussions on this subject. In spite of this, it is claimed that certain structures can be recognized as persistent fœtal tissue, firstly from their histological similarity to those in the fœtal kidney, secondly by their independence of superadded disease, and thirdly by their association with congenital anomalies of the urinary tract. They are specified below, and it is instructive to find that each has been described either in ' hypoplastic ' kidneys (some of which seem to have been infected) or as specific features of the fœtal kidney itself.

*Table I.*—Details of 12 Cases

The Occurrence of Persistent Fœtal Tissue in each Case

| Case | Age | Normal Renal Tissue | Hydronephrosis or Hydrocalix | Period of Infection | Hypertension | Delta-like Medulla | Primitive Tubules | | | Glomeruli | | | Interstitial Tissue | | Capillary Network | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | In Medulla | Cortico-medullary | Subcapsular | Rudimentary | Cystic Capsule | Infantile | Primitive | Concentric Arrangement | | |
| 1 | 1 day | + | + | ○ | + | + | + | + | + | + | + | + | + | + | + | No normal tissue in R. Kidney |
| 2 | 2 days. Premature | + medulla | ○ | ○ | ○ | + | + | + | + | + | + | + | + | + | + | |
| 3 | 1 hr. | ○ | ○ | ○ | ? | ○ | + | + | + | + | + | + | + | ± | + | |
| 4 | 3 wk. | + | + | ○ | ? | ○ | + | + | + | + | + | + | + | + | + | No normal tissue in L. No subcapsular primitive tubules found in R. |
| 5 | 7 mth. | + | + | 4 mth. | + | ○ | ± | ○ | ± | + | + | + | ? œdema | ○ | + | |
| 6 | 2 yr. | + | + | 1 mth. | + | + | + | + | + | + | ○ | + | + | ○ | ○ | |
| 7 | 3½ yr. | + | ○ | ○ | + | + | + | + | ○ | + | ○ | + | + | ○ | ± | |
| 8 | 5½ yr. | + | + | 3 mth. | + | + | + | ○ | ± | ○ | ○ | ○ | + | ○ | ± | |
| 9 | 6 yr. | + | + | 2½ yr. | + | + | + | ? infected | + | + | ○ | ○ | + | ○ | + | |
| 10 | 9 yr. | + | + | 7½ yr. | + | + | + | + | + | + | + | ○ | + | ○ | + | |
| 11 | 11 yr. | + | ○ | ○ | ? | + | + | ± | ± | ○ | ○ | ○ | ± | + | + | |
| 12 | 11 yr. | + | + | 7½ yr. | + | + | + | ? infected | + | ○ | ○ | ○ | ○ | + | + | |

+ = present ± = very slight ○ = absent

1. *Primitive Tubules.*—Eisendrath (1935) and Hyman (1937) both describe these structures as remnants of the Wolffian duct, and there is an excellent photograph of them in the treatise written by Baggenstoss (1951). The narrow columns of cells without any lumen resemble Braun's cords (Minot, 1892).

2. *Rudimentary Glomeruli.*—These are mentioned by Gutierrez (1933) and by Eisendrath (1935). Herxheimer (1909) suggested that failure of synchronous development of the epithelial and mesenchymal portions of the Malpighian corpuscles may lead to the formation of a hyaline structure. Congenital glomerulosclerosis is described by Friedman, Grayzel, and Lederer (1942). In the present paper these latter two types are not considered to be persistent fœtal structures, but reference is made to them in *Table II*. The infantile glomerulus should not persist beyond the second year (Gruenwald and Popper, 1940).

3. *Interstitial Tissue.*—Abundant cellular tissue separating the tubules is described by Minot (1892) as especially characteristic of the fœtal kidney. Arrangement around primitive structures in concentric layers was noted by Baggenstoss (1951) and thought to be muscle by Cicchino, Yates, and Chappell (1951).

4. *The Capillary Network.*—This appearance was described in the fœtal cortex by Minot (1892).

*Table II.*—Histological Features not Recognizable as Fœtal Tissue

| Case | Age | Period of Infection | Cortical Scars | Hydronephrosis | Hypertension | Glomeruli | | Tubules | | | | Interstitial Tissue | | | | | Arterioles and Arteries | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Simple Fibrotic Tufts | Pericapsular Concentric Fibrosis | Thyroid-like | Atrophic | Tubular Cysts | Cellular Casts | Lymphocytic Infiltration | Plasma-cell Infiltration | Polymorphonuclear Infiltration | Lymphoid Follicles | Fibrosis | Intima Thickened | Muscle Thickened | Malignant Hypertension | Hyaline Degeneration |
| 1 | 1 day | ○ | + | + | + | ○ | ○ | ○ | + | ○ | ○ | ○ | ○ | ○ | ○ | + | ○ | ○ | ○ | ○ |
| 2 | 2 days premature | ○ | + | ○ | ○ | ○ | ○ | ○ | ○ | + | ○ | ○ | ○ | ○ | ○ | + | ○ | ○ | ○ | ○ |
| 3 | 1 hr. | ○ | + | ○ | ? | ○ | ○ | ○ | ○ | + | ○ | + with hæmopoiesis | ○ | + hæmopoiesis | ○ | ○ | ○ | ○ | ○ | ○ |
| 4 | 3 wk. | ○ | ○ | + | ? | ○ | ○ | ○ | ○ | + | + | ○ | + | ○ | + | + | ○ | + | + | + |
| 5 | 7 mth. | 4 mth. | + | + | + | ○ | ○ | + | ○ | + | + | ○ | + | ○ | + | + | ○ | + | + | + |
| 6 | 2 yr. | 1 mth. | + | + | + | ○ | ○ | ○ | + | ○ | + | + | + | + | + | + | ○ | + | + | + |
| 7 | 3½ yr. | ○ | + | ○ | + | + | + | + | ○ | + | + | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 8 | 5½ yr. | 3 mth. | + | + | + | ○ | ○ | + | ○ | + | + | + | ○ | ○ | ○ | + medulla | ○ | ○ | ○ | ○ |
| 9 | 6 yr. | 2½ yr. | + | + | + | + | + | + | + | ○ | + | + | + | + eosinophil | + | ○ | ○ | + | ○ | ○ |
| 10 | 9 yr. | 7½ yr. | + | + | + | + | + | + | ○ | ○ | + | + | ○ | ○ | + | ○ | + | + | ○ | ○ |
| 11 | 11 yr. | ○ | + | ○ | ? | ○ | ○ | ○ | ○ | ○ | ○ | + | ○ | ○ | ○ | + | ○ | + | ○ | ○ |
| 12 | 11 yr. | 7½ yr. | + | + | + | ○ | + | + | ○ | ○ | ○ | + | ○ | ○ | ○ | + medulla | + | + | + | + |

+ = present ± = very slight ○ = absent

Eisendrath (1935) refers to thick-walled small arteries, but Bell (1950) regards this as a degenerative change.

5. *The Delta-like Medullary Pyramid.*—This feature is included with diffidence because I have found no direct reference to it. It has been suggested previously that it may be related to a failure in the process of reduction of certain generations of tubules in the formation of a normal pelvis, a developmental error suggested by Eisendrath (1935).

A study of *Table I* will show that the presence of none of these structures is solely related to infection, hydronephrosis, or vascular disease. In other words, the microscopical appearances which I believe to be fœtal tissue are found both in the presence and in the absence of these secondary conditions. It is therefore unlikely that they result from the effect of such diseases. It is assumed that chronic or healed pyelonephritis cannot be present in *Cases* 1, 2, 3, and 4, and this is supported by the absence of any cellular infiltration in the kidneys (*Table II*).

Finally, it seems reasonable to suppose that gross congenital abnormalities such as are present in some of these kidneys may be accompanied by structural defects in the parenchyma.

It might be thought that animal experiments would enable the histological features of pure infection to be distinguished from those of maldevelopment. In a review of the published work, Horn (1937) states that focal scars in the renal cortex are found in an average of 40 per cent of normal dogs and rabbits. Whatever their origin, such lesions might give rise to confusion in the elucidation of the histology of experimental pyelonephritis. This difficulty does appear to have been met by descriptions of an adequate number of controls (Mallory, Crane, and Edwards, 1940; de Navasquez, 1950).

The term 'hypoplasia' has already been used, but only in reference to previous publications. Baggenstoss (1951) discussed the nomenclature of congenital anomalies of the kidney and his terminology is reasonable and clear. The kidneys described in this paper are regarded as dysplastic, some of them having a superimposed infection.

There seems no reason to suppose that foci of maldevelopment must be confined to kidneys which show gross congenital anomalies, and it is suggested that the kidneys of 'non-obstructive pyelonephritis' (Bell, 1950) are infected because they are dysplastic. Persistent fœtal structures can occasionally be recognized in such kidneys from adults, but this material is very difficult to obtain. No attempt is made in this paper to specify the effect of age or disease on persistent fœtal tissue. The incidence of additional histological features is recorded in *Table II*. It is considered that the scars are just as likely to be the result of developmental defect as they are to be due to infection; both factors may play a part.

In this connexion it may be noted that local ischæmia is considered to be an important factor in the establishment of infection (Payling Wright, 1950), and since it is the foci of dysplasia which become infected, they may well be relatively ischæmic. This might be regarded as further evidence of the hæmatogenous route in renal infection.

It will be observed that there was arterial hypertension in all the cases in which the blood-pressure was recorded. Too much emphasis is not placed on this because the normal values are not universally agreed and there are technical difficulties in measuring the blood-pressure of children, but such uniformity deserves comment. Reference has already been made to a proved example of neonatal hypertension similar to *Case* 1, and in *Case* 7 there was nothing to suggest past or present infection; in 2 cases, therefore, hypertension was found in the absence of pyelonephritis. The literature contains many examples of congenital anomalies of the kidney associated with arterial hypertension (Abeshouse, 1941), and it is suggested that in the cases reported in this paper, renal dysplasia bears a relationship to the raised blood-pressure similar to that here attributed to it in the establishment of pyelonephritis.

## SUMMARY

1. Structures resembling those of the fœtal kidney have been found in infected kidneys of children.

2. From a series of cases, in some of which pyelonephritis, hydronephrosis, and vascular disease were undoubtedly present, either separately or together, it has been possible to show that none of these conditions could be uniquely responsible for the histological appearances.

3. Other histological features found in macroscopic scars in these kidneys are tabulated, and it is concluded that at least some of them are congenital in origin, though not recognizable as fœtal tissue.

4. It is therefore suggested that focal or localized dysplasia of the renal parenchyma is commonly the underlying lesion in pyelonephritis.

5. The liability of these dysplastic foci to become infected may be due to relative ischæmia.

6. Since most of these cases are thought to have been hypertensive, it is suggested that there may be a relationship between the primary condition of dysplasia and the subsequent appearance of arterial hypertension.

I am greatly indebted to Mr. Guy Baines, Dr. H. Everley Jones, Dr. H. S. Baar, Mr. W. R. S. Hutchinson, and Dr. K. M. Carmichael, who so kindly supplied me with the material for this investigation.

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# RETICULUM-CELL SARCOMA OF SMALL INTESTINE WITH PERFORATION

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THE case recorded here is believed to be unique in having had three separate perforations, at intervals of several months, of a type of lesion which is itself rather rare.

## CASE REPORT

R. V., aged 45, employed as one of a fire prevention squad at a very large petrol refinery, first had symptoms referable to his alimentary tract in June, 1949, about a month before his first admission to hospital. At that time he had mild lower abdominal pain, with some nausea and vomiting. Apparently his doctor had regarded him as a 'settling appendicitis' when he saw him, and he had not had to go off work. From then until the time of his admission he had had slight abdominal discomfort. His previous history included three bouts of pneumonia, the most recent a year previously. There was no history of injury to the abdomen, nor of typhoid fever or dysentery. There was a very vague history of some flatulent dyspepsia in February, 1948. His work did bring him into contact with petrol fumes at times.

FIG. 79.—Tinted photograph of the specimen removed at operation in November, 1949.

FIRST ADMISSION (July 2, 1949).—A severe attack of lower abdominal pain occurred at 1.30 p.m. about half an hour after his midday meal, followed by vomiting; the pain was continuous with colicky exacerbations. He tended to lie on his right side. The abdomen was tender and rigid all over when seen four and a half hours later. The diagnosis of general peritonitis was obvious.

*At laparotomy*, the diagnosis of general peritonitis was at once confirmed, but its origin was not immediately apparent. Appendix, stomach and duodenum, gall-bladder, and colon were normal. Some enlarged mesenteric glands were noted. Finally a perforation, about ⅛ in. in diameter, of the jejunum was found 2–3 ft. from the duodenojejunal flexure. This perforation had a considerable amount of induration around it. After taking a small section for biopsy the perforation was closed by invaginating sutures, and the peritoneal cavity was closed with drainage. Convalescence was prolonged by an acute bronchopneumonia. A Widal taken on July 4 was negative in all dilutions to typhoid and paratyphoid A and B. Dr. MacLean, the pathologist, reported on the biopsy specimen that it showed a spindle-celled sarcoma.

*Second Operation* (July 28).—The abdomen was re-opened through a fresh incision. About 18 in. of jejunum was resected with end-to-end restoration of continuity. This portion of bowel contained the growth, which had perforated, and three other small growths proximal to it. Enlarged glands were noted in the mesentery, but owing to their very close proximity to the superior mesenteric artery not all of them could be removed in the specimen. No other lesions were noted elsewhere in the bowel, and the liver was free of secondaries. The patient was discharged from hospital on Aug. 16, apparently well.

The patient was seen at out-patients on Oct. 7 and then professed himself well. No physical signs of recurrence could be detected.

SECOND ADMISSION (Nov. 17).—Again there were typical signs of general peritonitis occurring a few hours before re-admission. He had had some premonitory abdominal discomfort for fourteen days previously.

*Third Laparotomy*.—The perforation on this occasion was about 3 ft. from the duodenojejunal flexure, and its immediate surroundings were this time very suggestive of malignancy. About 9 in. of jejunum were resected (to include an unperforated growth a little lower down) and continuity restored by end-to-end anastomosis. There did not appear to be any secondaries in the liver. The enlargement of the mesenteric glands was still present, but without further increase. (*Fig.* 79.)

Again recovery was delayed by chest complications, but ultimately he did very well and was discharged on Dec. 14. The question of deep X-ray therapy was now considered, but the radiotherapists advised against it.

A fractional barium meal carried out in January, 1950, failed to reveal any abnormality in the small intestine.

THIRD ADMISSION (Feb. 22, 1950).—The patient's history this time was one of vague abdominal discomfort together with much cough and sputum. He was thought

to have had an influenzal attack. However, he passed some blood per rectum on one occasion. Re-examination, however, revealed no abnormal physical signs and the patient was unwilling to undergo exploratory laparotomy. X-ray examination of the chest was clear. He was discharged on March 4.

FOURTH ADMISSION (March 7).—An attack of upper abdominal pain occurred shortly before he came in, but on this occasion there was no evidence of peritonitis. By this time the patient was getting very tired of hospital and apart from X-raying his lumbar spine and pelvis, nothing more was done. These radiographs were normal. He was discharged on March 15.

FIFTH ADMISSION (April 9).—Again symptoms of general peritonitis appeared suddenly as in his first and second admissions.

*Laparotomy* through the original scar was carried out and the perforation this time was about 2½ ft. from the duodenojejunal flexure. There were several other unperforated growths palpable. About 3 ft. of the jejunum was resected, continuity as before being restored by end-to-end anastomosis. On this occasion a further effort was made to remove the mesenteric glands, which were enlarged. A doubtful lesion was palpable now in the ileum, but I did not feel that he would stand any further resection at this time. As usual, he had much chest trouble in convalescence, together, this time, with suppuration in the wound. He seemed fairly well when he was discharged on May 9.

Following this operation he made good progress and even returned to work for a short time.

SIXTH ADMISSION (Dec. 7).—For the three months prior to this admission he had been steadily going down hill, with few specific symptoms at first. About a fortnight before re-admission he had had another severe attack of abdominal pain, but had declined to come into hospital again, and to his doctor's surprise had gradually recovered from that. On the morning of admission he had been wakened by a desire to micturate and on doing so had experienced great pain: he noticed fæces and air bubbles in his urine. By this time the patient's condition was obviously desperate and on Dec. 12 he died.

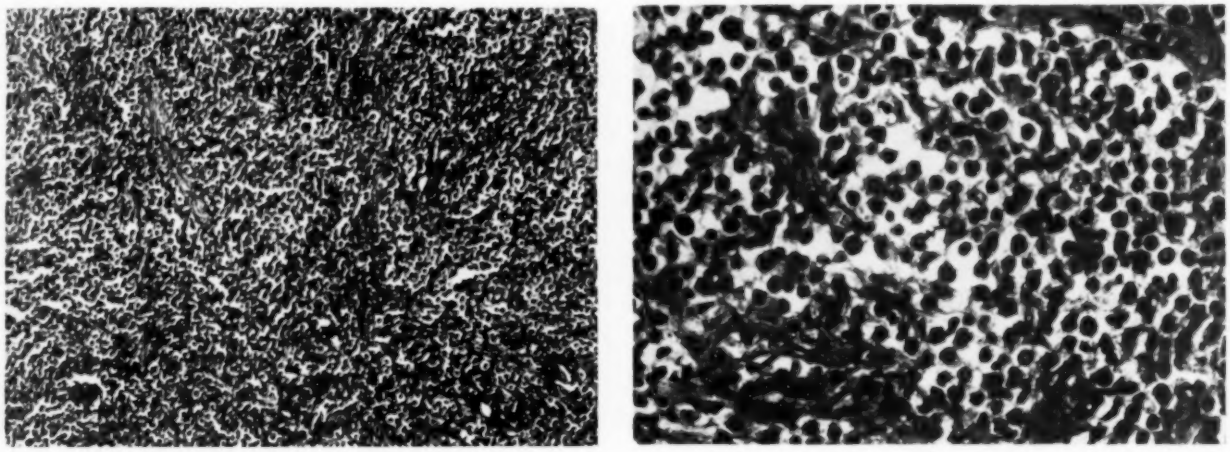
*Necropsy Report* (Dr. H. MacLean and Dr. Parry).—External examination of the body—slight emaciation. The skin was dry and in parts brown and scaly, suggestive of a vitamin deficiency. There were some dilated venules over both knees. On the abdomen there were three healed surgical scars.

*Head and Neck*: Tongue, larynx, thyroid normal, enlarged retropharyngeal glands.

*Thorax*: There were many adhesions between the left lung and the parietal pleura, and there was some straw-coloured fluid (100 c.c.). The right lung was adherent posteriorly to the chest wall and there was 200 c.c. of free fluid in the right hemithorax. The lower lobe of the left lung contained, towards its periphery, some neoplastic deposits, the largest being about 1½ in. in diameter and there were a few smaller nodules in the vicinity. The upper lobe contained no tumour. Above the area of the growth there was extensive evidence of bronchopneumonia in the lower lobe. The right lung contained, near the hilum and situated in the apical portion of the lower lobe, a mass of growth measuring about 1 in. in diameter.

The remainder of the right lung was normal macroscopically. The hilar glands were markedly enlarged, the left being approximately 3 in. long by 1 in. by ¾ in.

The cut surface was firm and grey and contained carbon particles. Macroscopically this was a malignant gland. The gland in the right hilum was not so large, but was, nevertheless, involved in malignant growth. The left lung weighed 29½ oz., the right lung 33¾ oz.



A B

FIG. 80.—Section from specimen shown in *Fig.* 79. A, Low-power view (× 80). B, High-power view (× 280).

*Cardiovascular System*: The pericardium was normal. There was some slight increase of pericardial fluid of normal appearance. The heart weighed 9 oz. The heart was soft and flabby and on the epicardial surface there were milk spots. The ventricles, auricles, and endocardium were normal. The valves and the coronary arteries showed no evidence of disease. The aorta was healthy.

*Abdomen*: There was a small amount of ascitic fluid which was not measured but would probably be about 3 oz.

The stomach and duodenum showed no obvious abnormality. About 18 in. from the duodenojejunal flexure the gut was adherent to another piece of small intestine, and, on attempting to separate the two, it was found that the wall in this area had broken down and the edges of the lesion were thickened. No other lesions were found in the jejunum. The ileum at a point 15–18 in. from the ileocæcal valve was kinked and twisted and firmly adherent to the bladder, into which there was a large fistulous opening; it was possible by introducing a finger from the bladder side to distinguish the efferent and afferent loops of ileum, and a short distance from these there was a fistulous opening between two pieces of the ileum and the walls of these openings were thickened.

The large intestine was normal as far as the sigmoid colon, where it became bound up in the adhesions around

the vesico-ileal fistula. The liver weighed 67 oz., but showed no gross abnormalities. The gall-bladder was distended with thin bile, but was otherwise normal, and the bile-ducts were patent.

The spleen weighed 6 oz. and appeared to be normal. The adrenal glands and the pancreas appeared normal. The mesentery contained many small glands.

*Genito-urinary System*: There was no obvious abnormality of the kidneys, which weighed 8 oz. each.

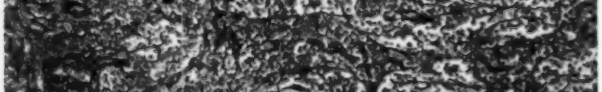


FIG. 81.—Section from same tumour, with silver staining, to show fibrils. (× 80.)

The ureters, although they passed beneath the inflammatory mass in the pelvis, were significantly normal.

The bladder contained fæces and the mucosa was brown and polypoidal in nature. The fistulous opening was towards the left and above the trigone. The prostate appeared to be normal.

Microscopical examination of the tissues removed at the operation in November, 1949, was considered to reveal a reticulum-cell sarcoma. Typical portions of the slides under low and high power are shown in *Fig.* 80. *Fig.* 81 shows a portion of the same tumour after silver staining to demonstrate the fibrillar formation.

## COMMENT

Most surgeons consider malignant disease of the small intestine to be rare. Yet most surgeons have met a few cases at least of the condition and the increasing number of articles in surgical journals on this subject shows that interest in it is growing. Perusal of these articles gives the impression that most of the malignant tumours described (at least, of those which were operable) were carcinomatous. A recent article by Maria Pepe (1950) states that about 600 cases of sarcoma of the small intestine have appeared in the literature. To gain some idea of the frequency with which the condition is diagnosed I have consulted the Registrar-General for England and Wales, whose deparment has kindly given me the following figures: In 1949, there were 509,973 deaths from all causes, and of these 142 were ascribed to cancer of the small intestine. Only 19 of these 142 cases were said to be sarcomatous; the rest, apart from 11 undefined, were due to carcinoma. The Registrar-General was unable to state in how many of these cases the diagnosis was based on autopsy or operation. This condition, however, is not likely to be diagnosed without one or other of these methods and we may, therefore, regard the 19 cases as a minimum figure for the annual incidence of the condition. The point is worth emphasizing that even at operation malignant disease of the small bowel may quite easily be overlooked. Thus H. K. Sowles (1934) has described 2 cases in which this occurred; adhesions and gall-stones were respectively dealt with at operations carried out for symptoms which were later proved to be due to malignant disease of the small intestine. T. M. Joyce (1934) describes a similar case when chronic appendicitis was mistakenly dealt with. The case described in this paper was very naturally thought to be a 'grumbling appendix' for a month before he was sent to hospital. It is doubtless easy enough to come on the large tumours, but deliberate palpation of the whole length of the small intestine is necessary to detect some of the smaller lesions. Certainly one suspects that belief in the rarity of these tumours leads to very many of them being overlooked.

The classification of intestinal sarcomata is in confusion. In view of the smallness of the series which can be studied at any centre this is not surprising. I have used the term 'reticulosarcoma' in accordance with the definition of the term reticulum-cell sarcoma given by Willis (1948): "The term 'reticulum-cell sarcoma' is, however, more strictly applied to tumours in which the predominant or only line of differentiation of the neoplastic cells is towards reticular connective tissue, i.e., to fibrifying tumours allied to fibrosarcomas. It has also been extended to include the undifferentiated or anaplastic syncytial reticulosarcomas, which, however, are not sharply separable from other anaplastic sarcomas or lymphoid tissue—'Hodgkin's sarcomas' and primitive lymphoblastomas. As regards all of these anaplastic growths indeed it is necessary to recall . . . that their very anaplasia renders attempts to subdivide them inadvisable".

Ewing (1940), on the other hand, tended to equate the terms 'reticulum-cell sarcoma' and 'large round-cell lymphosarcoma', emphasizing that the reticulum cells arise from the germ centres of lymph follicles. Willis's use of the term makes for greater clarity and has been here followed. The formation of fibrils in the tumours here described is well seen in the microphotograph of the silver preparations (*Fig.* 81). Only a few cases of reticulum-cell sarcoma of the small intestine have been reported as such in the literature. The diagnosis was seldom used until 1940. Its relationship to lymphosarcoma is apparently close, but quite indefinite. Doubtless most of the cases have been grouped with the lymphosarcomas, as for example by Ullman and Abeshouse (1932) and by Warren and Lulenski (1942) in reviewing large series of lymphosarcomata. Usher and Dixon (1943) reviewed all the cases of lymphosarcoma of the small and large intestines available for study at the Mayo Clinic. There were 50 such cases, and these authors were able to divide them into 25 cases each of malignant lymphocytoma (or small round-cell sarcoma) and of reticulum-cell sarcoma; as a result of this review they concluded that there were no essential differences between the two types of growth. Their histological criteria, however, were based on cell shape and structure; they do not appear to have examined all their reticulum-cell

sarcomata for the presence of fibrils, and in 4 in which they did so they report that they failed to demonstrate this feature. There is, therefore, little information as to the normal course of these reticulum-cell tumours. Fraser (1945) has, however, given brief details of 3 cases of reticulum-cell sarcoma with notes of post-mortem findings in one of them. In none of these was a mass palpable, and the growth was of an infiltrative character. In the case in which a post-mortem examination was made, a second growth, not ulcerated, was discovered in the small intestine at a distance of some feet from the first. Frank, Miller, and Bell (1942) have also described a case in which histological diagnosis of reticulum sarcoma was made; their case presented as a chronic intestinal obstruction; a solitary large tumour of the jejunum was found and successfully resected, and the patient was alive and well nine months later.

Perforation of a neoplasm of the small intestine is commonly mentioned as a complication in systematic accounts of these tumours. In fact it is rather uncommon, and when it does occur it is quite commonly the terminal event of large tumours which have undergone necrosis and ulceration. Such is the impression given by perusal of published cases. Perforation seems to be relatively commoner in carcinomata than in sarcomata. Instances of true perforation of a sarcoma of small intestine have been recorded by Whittaker and Fisher (1934), Eli Davies (1937), D. L. Lewis (1939), Frank, Miller, and Bell (1942), K. Fraser (1945), R. H. Cowdell (1950), and T. H. Cullen (1950). All but two of these cases died within a few hours of admission to hospital. The case presented in this paper, in which perforation occurred on three occasions from different neoplasms, is apparently unique.

Multiplicity of malignant lesions in the small intestine is known to occur under certain conditions. The best-defined group is that of the carcinoids. Multiple polypi may occur and undergo malignant transformation (Wakeley and Paul, 1931). A case of ganglioneuromatosis has been described by Poate and Inglis (1928) in which three separate coincident tumours were present; and J. D. Collins (1944), in an account of neurofibromata of the intestine, mentions one case with multiple malignant lesions. Occasionally melanomatous secondaries seem to select the small intestine for the main site of metastasis, as in a case seen in this hospital recently. D. Robb (1929) has given a report of 2 such cases. McSwain and Beal (1944) record a case in which there were three separate simultaneous neoplasms of the upper end of the jejunum causing partial obstruction; these lesions were about 15 cm. apart, and about 40 cm. of jejunum was excised. The diagnosis in their case was large-cell lymphosarcoma, in preference apparently to a diagnosis of reticulum-cell sarcoma. Warren and Lulenski (1942), who recognized certain intestinal tumours as reticulum-cell sarcomata but decided not to distinguish these from lymphosarcomata, noted that lymphoid tumours in some intestines did produce discrete lesions here and there in the bowel; but unfortunately no details of these appear in their paper.

Multiple lymphoid lesions in the intestine raise the possibility of them all being secondary tumours, but in the case reported in this paper there were neoplasms in only two organs, the small intestine and the lungs. The clinical course seems to point conclusively to the small intestine as the primary site, but it remains debatable whether the series of growths in the small intestine arose independently of one another or whether the later growths were in fact secondaries. If the latter possibility is accepted the path of dissemination remains speculative. Transmission of malignant cells along the intestinal lumen and their implantation lower down is a theoretical possibility which has never been seriously investigated. On the other hand, lymphatic pathways in the submucosa might be adequate to account for the spread, but it then remains surprising that no convincing evidence of metastasis in the mesenteric glands could be found. It is therefore believed that this case is an instance of primary multiple discrete reticulum-cell sarcomatosis of the small intestine.

I am indebted to Mr. M. Silverstone for his advice and help in the treatment of this patient, and Dr. Hugh MacLean for the pathological reports and much help with the histology.

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# PLASMOCYTOMAS PRODUCING PARAPLEGIA*

BY LAMBERT ROGERS, CARDIFF

PLASMOCYTOMAS or myelomas, especially when of the so-called solitary variety, constitute one of the less frequent causes of paraplegia produced by compression of the spinal cord. During the past few years 4 such cases have been admitted to this Unit, 3 in men aged 47, 61, and 68, another in a married woman aged 37. Brief notes of the case-histories are :

*Case* 1.—Mrs. S. P., aged 37, transferred from the Prince of Wales Orthopædic Hospital (Mr. A. O. Parker) with pain in the back of ten months' duration and recent paraplegia. The right leg began to drag and later she lost the use of both legs and control over the sphincters. There was a small gibbus at the level of the tenth thoracic vertebra and radiographs showed absorption of the body of this vertebra. Bence-Jones proteose was present in the urine. On Sept. 30, 1948, laminectomy revealed a fleshy, granular, extradural tumour extending into the erector spinæ muscle masses and compressing the cord at this level. She recovered following operation, but died some two years later from bronchopneumonia complicating multiple myelomatosis. The report on the tumour tissue was plasmocytoma (*Fig.* 82). At autopsy, deposits of plasmocytoma were found in the right humerus, the skull, the sternum, and the third lumbar vertebra.

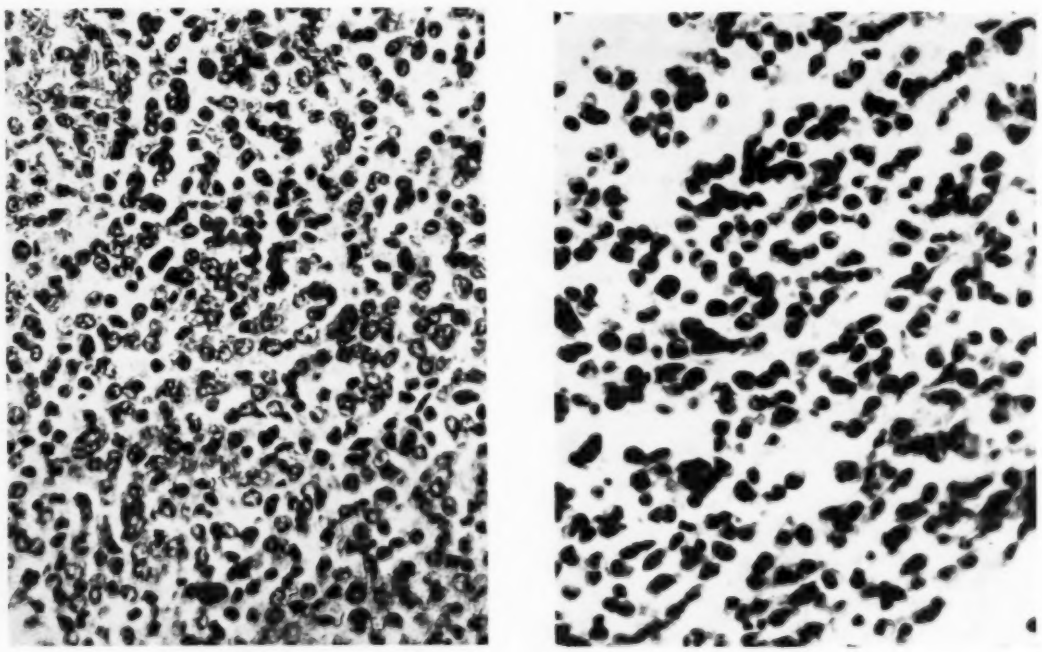

FIG. 82.—Microscopical appearances of spinal plasmocytoma from lower thoracic region of woman aged 37. A, × 360; B, × 456.

*Case* 2 (*Medical Unit, Professor Scarborough*).—F. L., aged 68, an underground colliery repairer, six months before coming under observation was involved in a fall of pit roof and had three ribs fractured. He later developed pain in the arms and legs and began to feel weak. He then had ' pins and needles ' in the feet and ankles and became incontinent and paraplegic. Radiographs showed translucent areas in some ribs and in the shaft of the left humerus. Bence-Jones proteose was not present in the urine. On May 9, 1950, laminectomy revealed a greyish, vascular, extradural tumour extending into the erector spinæ muscle masses at the level of the second thoracic vertebra. Following operation he showed some signs of recovery from his paraplegia, but died from an attack of coronary thrombosis six weeks later. The report on the tumour tissue was plasmocytoma (*Fig.* 83).

*Case* 3 (*Medical Unit, Professor Scarborough*).—A fortnight before admission to hospital, E. D. L., a retired miner, aged 61, working as a labourer, developed pain in the back and chest and ten days later had a feeling of ' pins and needles ' in his legs which soon became numb and paralysed. He was unable to pass urine, had a cough and breathlessness, and looked gravely ill. He was paraplegic, with increased knee-jerks and loss of sensation to pin-prick over the lower limbs and trunk as high as the umbilicus. Sternal puncture showed the presence of 40–50 per cent large myeloma cells. There was no Bence-Jones proteose present in the urine. On May 12, 1951, lower cervical and upper dorsal laminectomy was performed. Tumour masses were revealed extruding into the erector spinæ muscle masses, and there was extradural compression of the cord by tumour. He died thirty-six hours later from anoxia contributed to by massive pneumoconiosis. The report of the tumour was plasmocytoma (*Fig.* 84).

*Case* 4 (*Dr. J. D. Spillane*).—For seven months, R. F., a main line engine driver, aged 47, had backache which was worse when he was lying in bed, and when walking he had attacks of girdle pain. His legs and feet began to feel heavy and became weak and numb. Radiographs of the spine showed mild osteo-arthritis. There was diminished sensation up to the tenth thoracic spinal segment, and

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spasticity of the legs and exaggerated reflexes in the lower limbs were present. There was no Bence-Jones proteose in the urine. Myelography showed a hold-up of myodil at the upper border of the ninth thoracic vertebra. On Jan. 16, 1952, laminectomy revealed a fleshy tumour at this level. The tumour extended upwards for about 1½ in. and at this site the dura was compressed and not pulsating. After removal of the tumour, which encircled the theca, the dura was seen to be pulsating. He made a rapid recovery and by the end of the month was able to walk normally. The report of the tumour was myeloma (plasmocytoma) (*Fig.* 85).

*Follow-up Note*: On Oct. 10, 1952, this patient, who had been well in the interim and had completely recovered from his paraplegia, was re-admitted for the treatment of a hernia when it was noticed that he was anæmic (red cells 2,500,000; white cells, 4000). Bence-Jones proteose was now present in the urine, sternal puncture showed over 90 per cent of the cells to be myeloma or plasma cells, and radiographs showed some translucent areas in both femora. The condition had evidently become generalized in the months which had elapsed since the laminectomy. Treatment by nitrogen mustard was carried out by Dr. Leonard Howells.

## COMMENTS

All four patients had compression of the spinal cord by extradural plasmocytomas for which decompressive laminectomy was carried out. At the time of operation three of them had signs of the generalized disease—myelomatosis—but the other appeared to be an example of paraplegia produced by a solitary plasmocytoma. It cannot be certain, however, that the tumour was not an early and local manifestation of what was already the early stage of a generalized disease, and it is questionable whether cases of so-called solitary plasmocytoma do not in the course of time, and providing the patient lives long enough, all become examples of multiple or diffuse myelomatosis.

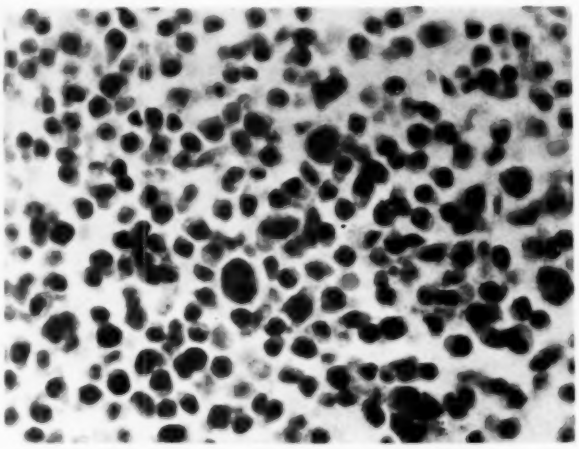


FIG. 83.—Microscopical appearance of spinal plasmocytoma from upper thoracic region of man aged 68. (× 425.)

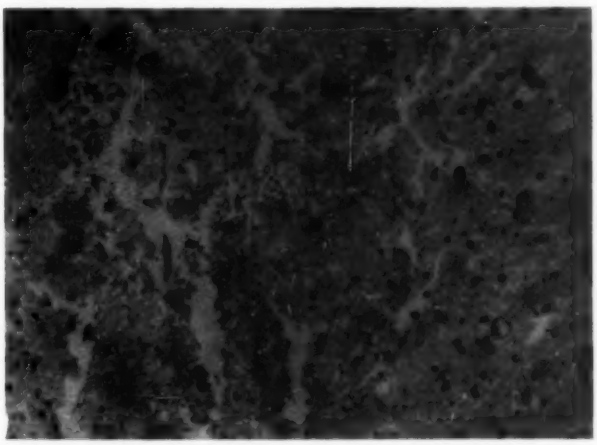
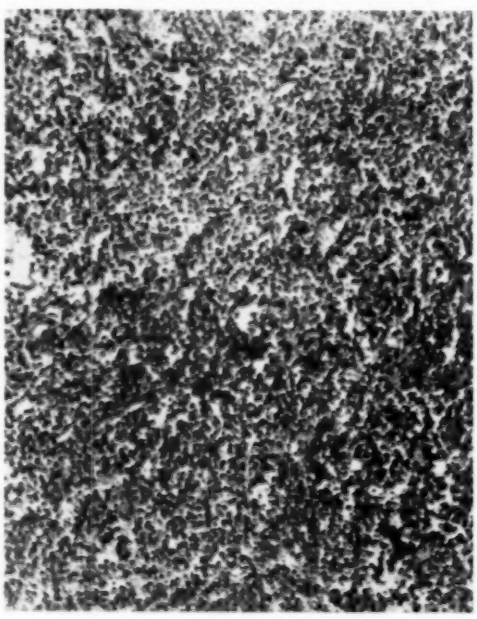
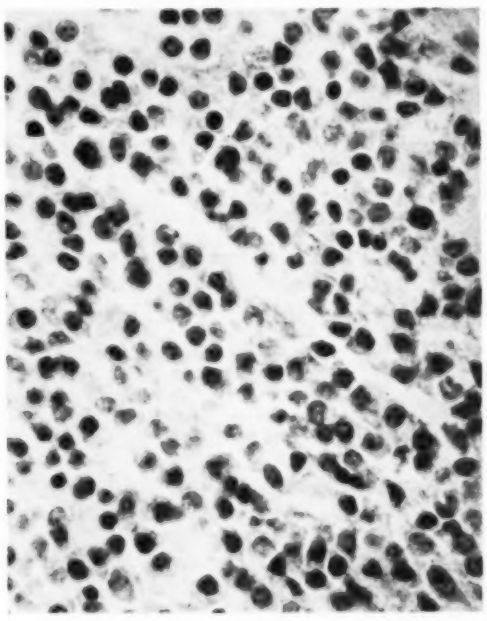


FIG. 84.—Microscopical appearance of spinal plasmocytoma from lower cervical region of man aged 61. (× 120.)



A



B

FIG. 85.—Microscopical appearances of spinal plasmocytoma from mid-thoracic region of man aged 47. A, × 32; B, × 500.

Shenkin, Horn, and Grant (1945) classified 7 of 54 lesions in the epidural space causing cord compression as myelomas; 6 of the 7 occurred in men. They noted that as a group these patients succumbed rapidly, the longest survival being 14 months. In 2 of their patients the vertebral lesion causing compression of the cord was an isolated one and 1 of these patients died three months after operation without showing evidence of other involvement, but in the other case radiographs showed changes in the ribs four months after operation. Raven and Willis (1949) reported a case of cord compression from a plasmocytoma in a man aged 56 with no recovery of paraplegia following laminectomy, and death six months later. At autopsy no other tumours were found. In such cases, however, we cannot know for certain whether the lesion is merely the forerunner of the systemic disease or is a true instance of a solitary plasmocytoma which is a distinct entity. In the fourth of our cases here reported, the engine driver aged 47, the tumour was solitary and after its removal the patient recovered well from his paraplegia, but ten months later, on returning to hospital to have a hernia operated upon, evidence was found of early but definite generalized myelomatosis. Lumb and Prossor (1948) record the case of a solitary tumour which existed for four years, during which many radiographic examinations of the skeleton were made and then general spread, typical of multiple myelomatosis, took place. Tennent (1945) reported a case of plasmocytoma which for 4½ years remained localized in the right ilium of a man, aged 53, and then became generalized, and in this case there had been no treatment of the lesion other than biopsy. Among 18 cases of solitary myeloma of bone reported by Cutler, Buschke, and Cantril (1936), 5 were known to have become generalized, but 2 with observed myelomas for four and ten years were alive without generalization.

*Conclusion*: The problem cannot yet be said to have been solved, but the available evidence is suggestive that in the course of time and if the patient survives long enough, a solitary plasmocytoma loses its title to be so called and the fate of the patient is to develop multiple myelomatosis.

## SUMMARY

Four cases of extrathecal compression of the spinal cord by plasmocytoma are reported. One patient who apparently had a solitary plasmocytoma at the time of operation, recovered from paraplegia following removal of the tumour and remained well for ten months, when other lesions appeared and he presented signs of myelomatosis, without, however, any return of paraplegia. Evidence is presented to support the view that the term 'solitary plasmocytoma' is usually only apparent or relative and that myelomatosis develops sooner or later in most of these cases.

I am indebted to Professors Jethro Gough and F. R. Magarey, of the Department of Pathology, for the reports on the specimens and for certain of the photomicrographs.

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# INTESTINAL OBSTRUCTION WITH CONGENITAL ABSENCE OF THE LEFT DIAPHRAGM

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CONGENITAL absence of a hemidiaphragm, almost invariably the left, is a rare condition, seldom intruding into surgical practice. The literature testifies to the fact that the condition is usually incompatible with life, and there are very few records of adult cases.

This case is of interest in the unusual presentation of intestinal obstruction with marked chest symptoms due to congenital absence of the left diaphragm. At the same time it shows that such atresia of the left diaphragm may be compatible with a long and healthy existence and may on X-ray examination be easily mistaken for Petit's eventration.

## CASE REPORT

Mr. H. Y., aged 79, was admitted to the Medical Wards on March 28, 1951. He had formerly led a normal active life and played strenuous games at school. At the age of 70 he developed symptoms of prostatic obstruction and a transvesical prostatectomy was performed at St. Mary's Hospital in 1942. From this he recovered well but attended a few years later with bronchitis and dyspepsia. During 1950 he was investigated for these symptoms and was found to have emphysema and "eventration of the left diaphragm" (*Figs.* 86, 87). The "left diaphragm" showed paradoxical movement and barium meal examination confirmed rotation of the stomach so that the greater curvature lay along the "left diaphragm" (*Fig.* 88). His out-patient notes in May, 1950, reported him as looking "remarkably fit for his age, then 78". On the evening of March 27, 1951, he noticed colicky pain in the lower abdomen and later became dyspnœic, with pain in the left chest. Since the onset his bowels were constipated and he passed no wind. He had vomited several times.

ON EXAMINATION.—Pulse 72; B.P. 150/100. Tongue dry and coated. Abdomen slightly distended. Borborygmi absent in abdomen. Trachea to right. Very poor movement of the left chest as compared with right, with increased resonance and very poor breath-sounds. No borborygmi were audible in chest. A diagnosis of spontaneous pneumothorax was made and an exploratory needle was inserted. The pressure was —12·6 c. mm. water and

500 c.c. of air were withdrawn, after which the pressure could not be registered. Radiography of the chest (*Fig.* 89) showed a high left diaphragm with an apparent pneumothorax associated with massive collapse of the left lung. The colicky abdominal pain continued, and it then became evident that the cause of the apparent pneumothorax was the presence of greatly distended loops of bowel in the left hemithorax, collapsing the left lung, consequent upon intestinal obstruction. Further X-ray examination on March 29, prior to laparotomy, showed the entire left hemithorax occupied by distended coils of gut, the mediastinum being shifted to the right and the left lung massively collapsed (*Fig.* 90).

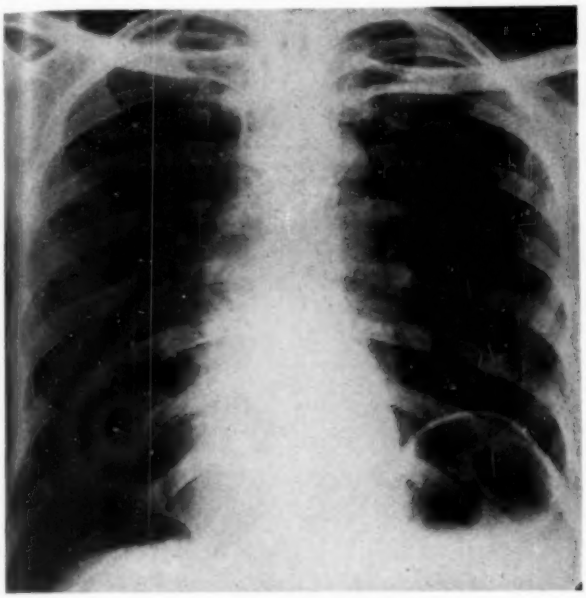

FIG. 86.—Radiograph of chest showing emphysema and 'eventration left diaphragm'. (April 28, 1950.)

FIG. 88.—Barium meal showing rotation of stomach. (May 12, 1950.)

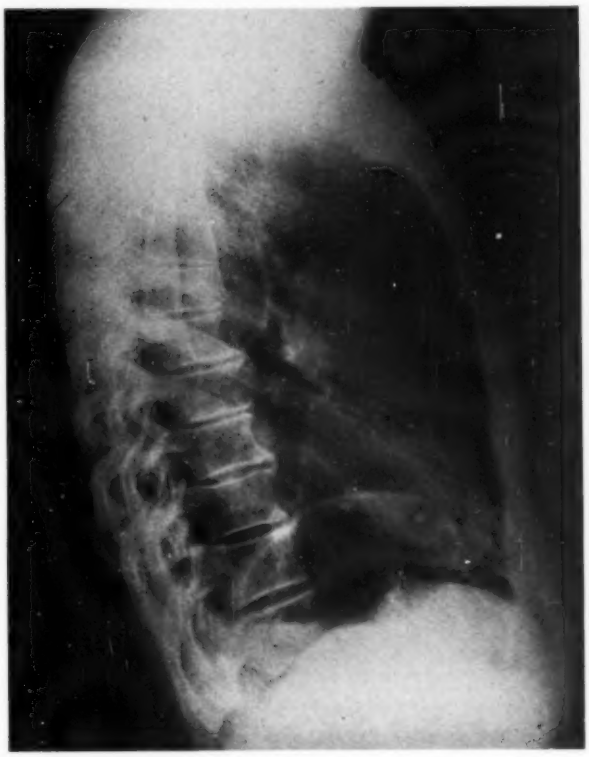

FIG. 87.—Lateral chest radiograph showing 'eventration of left diaphragm'. (April 28, 1950.)

AT OPERATION.—Laparotomy was performed sixteen hours after his admission, under spinal anæsthesia. Through an upper midline incision, obstruction of the ileum was found, which was due to an adhesion from the upper end of the prostatectomy scar to the root of the mesentery. Blood-stained fluid was present in the peritoneal cavity. The distended bowels had risen up into the left hemithorax and the left diaphragm was represented by a mere flange of tissue on the chest wall, such that it was possible to palpate the subclavian vessels at the apex of the left hemithorax without difficulty, and without the intervention of any membranous layer that might represent a left diaphragm. There was nothing to suggest that there had been rupture of a thin diaphragmatic leaf owing to the abdominal distension. The left diaphragm was virtually absent. The obstructing band was divided and the abdomen closed with interrupted deknatel sutures.

PROGRESS.—His post-operative course was marked by bronchitis and dyspnœa, but he began passing flatus well on the third post-operative day and, with the relief of his obstruction and distension, his dyspnœa improved; and at the same time radiographs of the chest showed re-expansion of the left lung, with the stomach and intestines receding back into the abdomen (*Fig.* 91). The *status quo ante* was almost restored when he was discharged from hospital three weeks after his admission. Radiography on May 7 showed good re-expansion of the left lung above the coils of bowel in the left lower chest (*Fig.* 92); on Oct. 12 it showed a return to the condition in 1950 except that the stomach was higher in

the chest and the mediastinum shifted more to the right (*Fig.* 93). On screening, the fundal region of the stomach was fixed and there was no respiratory excursion, and no radiological evidence of a left cupola. Presumably adhesions have formed to prevent the paradoxical movement seen in 1950. I.V.P. showed the kidneys to be normally situated.

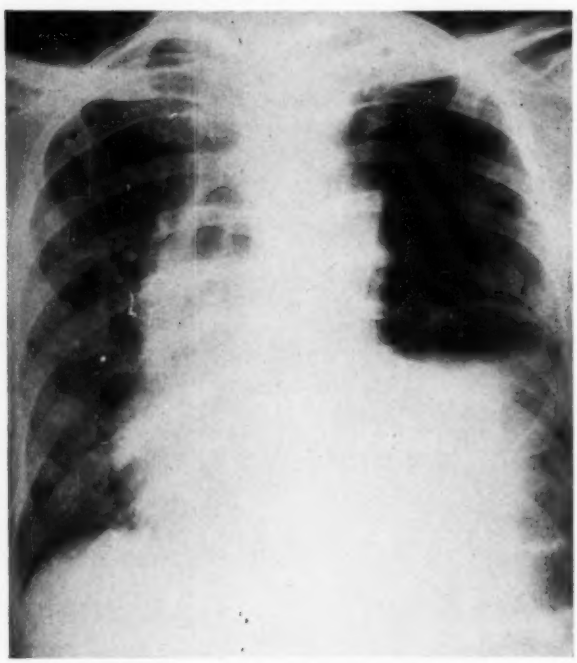

FIG. 89.—Distended bowels in left hemithorax with massive collapse of left lung, simulating pneumothorax. (March 28, 1951.)

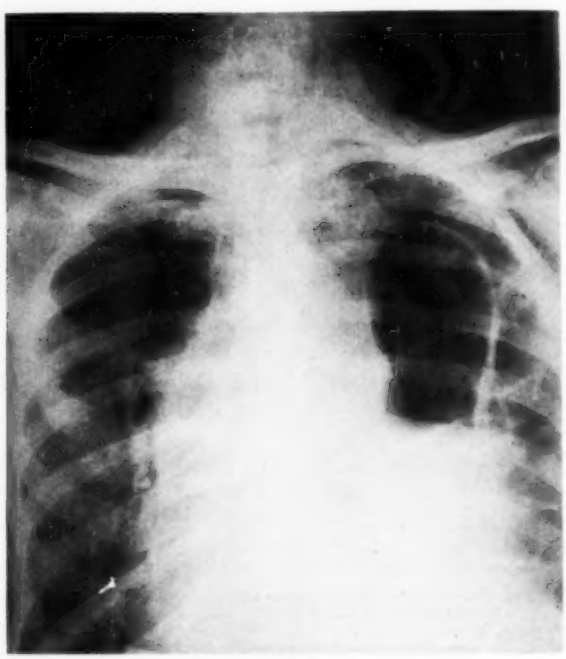

FIG. 90.—Distended coils in left hemithorax and mediastinal displacement to right. (March 29, 1951.)

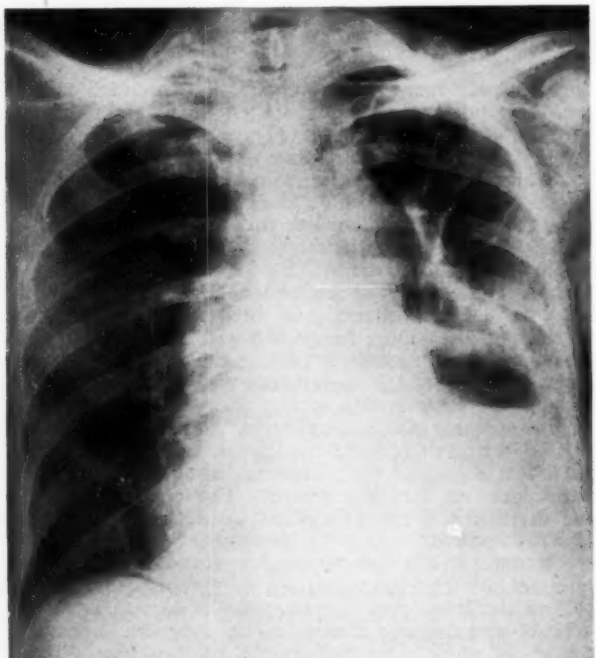

FIG. 91.—Obstruction relieved. Bowels less distended. Mediastinal displacement less. (March 30, 1951.)

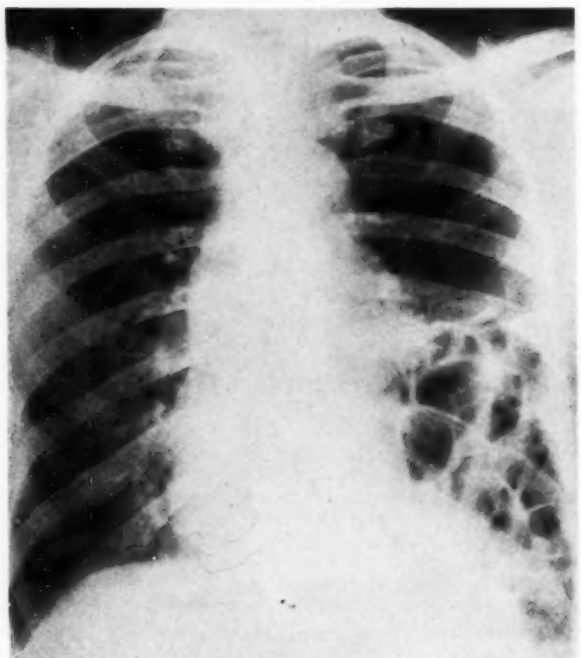

FIG. 92.—Left lung re-expanded. Mediastinum central. Bowels withdrawn into abdomen. (May 7, 1951.)

## HISTORICAL SURVEY

Sir Arthur Keith was one of the first to take an interest in this condition, and to describe the development of the diaphragm and its relation to the various types of hernia. In 1910 he recorded 3 cases of congenital absence of the left diaphragm in the fœtal

stage, and another case which lived to be over 70. In 1912 Wilfred Harris and Clayton-Greene described the first case coming to operation. In this case also pneumothorax was simulated. It occurred in a fat lady of 30 who complained of two years' aching pain in the left chest. She had previously had two fairly severe chest injuries, one with fractured ribs on the left side. The radiographs were interpreted as

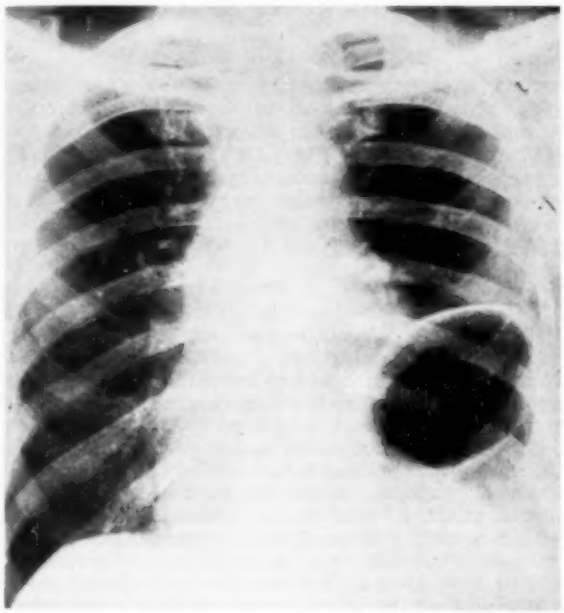

FIG. 93.—*Status quo* restored—stomach in contact with left lung. (Oct. 12, 1951.)

showing left pneumothorax and partial collapse of the left lung, but the clinical finding of borborygmi in the left chest led Dr. Harris to diagnose diaphragmatic hernia. At operation Clayton-Greene found the diaphragm absent, the stomach and intestines occupying the left hemithorax and compressing the left lung. Despite numerous adhesions it was possible to palpate the upper ribs via the abdominal incision. Operation would have been avoided in this case if the diagnosis had been more accurate.

J. B. Hume (1922) reviewed the condition and remarked that it was not infrequent in fœtal cases, being almost always incompatible with life. He referred to a case of a boy who lived to the age of 17. Hume stated that the whole diaphragm to the left of the œsophageal hiatus and the left crus was absent, with parietal pleura and peritoneum forming a continuous sheet. In 1927 Le Wald reviewed the condition from a radiological point of view and pointed out the difficulty of differentiating congenital absence from eventration, and sometimes from thoracic stomach. The case here recorded was reported previously as eventration. The critical examination is direct lateral screening which, in congenital absence, will show changes of contour, whereas in eventration, however high the 'diaphragm' has risen, the outline remains smooth and regular. Le Wald (1927) described 3 cases diagnosed radiologically. In the first the stomach was in the abdomen but the small intestine and proximal colon, in a non-rotated state, were in the left chest. This man was well at 37 and had formerly been a member of a successful 5-mile relay race team. The second, a woman of 62, had the stomach inverted in the chest, as in this case, together with the splenic flexure of the colon. The third, coming to necropsy at 47, again showed non-rotation of the colon, with the stomach and spleen and most of the colon, including the cæcum, in the left chest.

Further reviews by Barrett and Wheaton (1933) and by Dunhill (1934) agreed that congenital absence is most always incompatible with life, but in the same year Hackwood reported a case of a previously fit German girl of 20 who was operated upon for obstruction. The only viscera in the abdomen were the liver, pelvic organs, and descending colon. She died following operation, but no necropsy was obtained. Barclay in 1936 reported the case of a young footballer with the whole colon in the left chest. On screening there was perfect air entry into both lungs, the left lung expanding in a bizarre fashion around the bowels, as was also seen in this case. Stuart Harrington studied diaphragmatic hernia and published several fine reviews (1940, 1943, 1945). He found that a high percentage of children with congenital 'absence' of a hemidiaphragm suffer very early from cardiac and respiratory difficulty. He records that 75 per cent die in the first month and that many of the remainder die in childhood. He considers that it is unlikely that all the elements which normally help to form the hemidiaphragm are absent, but that there is failure of formation of that part derived from the Wolffian body. Thus there is a defect in the posterolateral part of the diaphragm extending from the 8th rib posteriorly and medially to the œsophageal hiatus. In those children who survive the cardiac and respiratory embarrassment which results, the chest wall grows away from the posterior margin of the defective diaphragm since the latter has no posterior attachment. Thus the defect increases in relative size as the child becomes older, and in the adult the remains of the diaphragm would probably be represented merely by a flange of tissue similar to that found at operation in the case recorded here.

There is no doubt, however, that in some cases, as recorded here, the lung and abdominal contents may find a *modus vivendi* and the subject live in good health and to a ripe old age. Dyspepsia and dyspnœa may occur, and there is a particular liability to intestinal obstruction. Radiologically pneumothorax must be differentiated, as must Petit's eventration. Operation is best avoided, as in Petit's eventration, unless other conditions such as obstruction or some other surgical emergency arise. The case here recorded illustrates the compatibility of the condition with normal active life, the usual misdiagnosis as eventration, and the simulation of pneumothorax which may occur. It is believed to be the oldest recorded case of congenital absence of the left hemidiaphragm and the only recorded case of advance and retreat of the bowels into the left chest consequent upon intestinal obstruction occurring in association with such a condition.

The patient has recently attended out-patients, having celebrated his eightieth birthday and having resumed playing golf!

I wish to thank Dr. E. Rohan Williams for the radiographs and Dr. P. N. Cardew for the photographic reproductions thereof.

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# PERFORATION AND OBSTRUCTION BY ENTEROLITH COMPLICATING JEJUNAL DIVERTICULOSIS

## A REPORT OF THREE CASES

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THE aetiology and the symptoms and signs of duodenal and jejunal diverticula have been fully reviewed by Fraser (1933), Mahorner and Kisner (1947), and Benson, Dixon, and Waugh (1943). That uncomplicated diverticula may merit surgical treatment is stressed by Mahorner and others, and more recently by Orr and Russell (1951), who make a plea for recognition of the condition as a cause of dyspeptic symptoms. All authors are agreed on the rarity of diverticulosis affecting the small intestine.

Where diverticulosis has been complicated by a local acute pathological condition, emergency surgery is often necessary, and the major complications have been reviewed by Milnes Walker (1945) and classified as follows :—

1. Acute diverticulitis, causing :
   *a*. General peritonitis.
   *b*. Localized abscess.
   *c*. Adhesions.
   *d*. Acute intestinal obstruction.

   These may or may not be associated with perforation.
2. Concretion formation, sometimes causing intestinal obstruction.
3. Hæmorrhage.
4. Traumatic rupture.
5. Volvulus.

To this list may be added :

6. Jaundice (Nicholson, 1935).

The incidence of complications is low, acute inflammation being the commonest, concretion formation being not uncommon, hæmorrhage and intestinal obstruction by an enterolith being rare.

I wish to place on record two cases of perforated jejunal diverticulitis and one case of intestinal obstruction by an enterolith which had presumably formed in a jejunal diverticulum.

## CASE REPORTS

*Case* 1.—Mr. W. M., aged 79, was admitted on Oct. 1, 1949, with a history of having had colicky central abdominal pain for 24 hours. The pain had been initially in the right iliac fossa and had later become generalized and constant ; he had had two loose motions, but, though complaining of nausea, had not vomited. He had had no previous abdominal symptoms.

ON EXAMINATION.—His tongue was furred and his temperature 99° F. and pulse 100. There was lower abdominal fullness, tenderness and guarding being maximal in the left iliac fossa. Clinically he was diagnosed as a case of atypical acute appendicitis.

OPERATION.—Through a right lower paramedian incision, free seropurulent exudate was found in the peritoneal cavity, but the appendix and pelvic colon were normal. On attempting to palpate the stomach, the omentum was found to be attached widely by old adhesions to the peritoneum of the anterior abdominal wall, and only after these had been separated was it established that acute jejunal diverticulitis was present. The diverticula were multiple and of varying size, ranging from ½ in. to 2 in. in diameter, distributed in the proximal 4 ft. One diverticulum, around which there was local œdema and fibrinous exudate, was covered by adherent omentum ; on separating this a pin-point perforation was found. It was invaginated with a purse-string suture and patched with a free omental graft.

Convalescence was uneventful, and the patient was discharged on Oct. 12, 1949.

*Case* 2.—Mr. J. C., aged 74, was admitted on Nov. 24, 1951, as an emergency, with a history of colicky central abdominal pain, associated with nausea, which had been present for three days. His bowels had last been open two days prior to admission. He had had two attacks of abdominal pain and vomiting, followed by diarrhœa, six and three years previously, each lasting about two days and resolving without treatment. Two months prior to admission, he complained of indigestion with epigastric pain occurring after meals ; this had become less severe in the three weeks preceding the acute attack which necessitated his admission to hospital.

ON EXAMINATION.—He was a thin old man and his general condition poor. Temperature 100° F. and pulse 120. There was some tympanitic fullness of the lower abdomen and tenderness with guarding was present maximally in the left hypochondrium, but there was a suggestion of a palpable mass in the left iliac fossa and rectal examination elicited a tender boggy fullness in the left rectovesical pouch. Clinically the diagnosis was in doubt, but acute jejunal diverticulitis was suggested as the most probable cause of his symptoms. It was decided that conservative treatment should be tried initially, the

stomach being kept empty by aspiration through a Ryle's tube, and fluid intake maintained by a rectal drip. Twelve hours after admission there had been no clinical improvement, the pulse-rate remaining 120, but the abdomen was more distended. In addition there was a fan-shaped area of hyperæmia over the left lower abdomen, radiating from the umbilicus, overlying the doubtful mass which had been palpated on admission. In view of the lack of response to conservative treatment, laparotomy was considered to be indicated.

OPERATION.—Through a left paramedian incision, coils of injected, dilated jejunum were found adherent to the peritoneum of the anterior abdominal wall, and on separating these, about 2 oz. of thick, white, slightly offensive pus were liberated from an abscess cavity, which lay immediately behind the parietal peritoneum. This had been responsible for the redness of the skin and the mass in the left iliac fossa. A perforated jejunal diverticulum was found to be the cause. To avoid dissemination of the infection no extensive exploration was undertaken, but some four to six further diverticula were identified both above and below the one which had perforated. By means of a purse-string suture and a free omental graft the perforation was closed, and the rectus sheath drained for 48 hours.

Convalescence was uncomplicated and the wound healed by first intention. The patient was discharged on Dec. 7 having been apyrexial for ten days. On account of a discharge from the wound, which had started four days previously, he was re-admitted on Dec. 17. His general condition was good, and he would not admit to having had pain. From a sinus in the wound there was a discharge of fluid intestinal contents and gas, and through the thin abdominal wall were visible waves of peristalsis, each wave being accompanied by a further intestinal efflux; the skin surrounding showed the excoriation which accompanies high intestinal fistulæ. Radiographs of his abdomen, taken in two planes, showed no gross jejunal dilatation or fluid levels, though the visible peristalsis indicated some degree of obstruction, and the sutured diverticulum had certainly leaked. Stricture formation or, more probably, kinking by plastic adhesions, following local peritonitis, were considered to be the most likely causes of incomplete obstruction. Treatment was conservative, and the patient's condition showed no deterioration, his appetite being unimpaired, and his bowels functioning normally each day. Spontaneous closure occurred four weeks after development of the fistula.

**Discussion.**—Acute diverticulitis, with or without perforation, appears to be the commonest complication affecting diverticula of the small intestine. Milnes Walker in his review quoted 19 cases from the literature and added a further 3 cases of his own. Benson and others (1943) describe 1 similar experience and Orr and Russell (1951) operated on a further 2 cases; to these may be added the 2 cases described in this paper. Mahorner and Kisner (1947) stress the importance of the surgeon being alive to the possibility of acute diverticulitis of the small intestine as a possible cause of peritonitis. Not only may symptoms be atypical, but free fluid or pus is often not found at laparotomy, the pus remaining localized in the early stages, though later, there is a marked tendency to spreading peritonitis. Boland (1939) describes a case where, though laparotomy revealed a peritonitis, no cause was found, until at the post-mortem examination it was shown to have originated in a perforated jejunal diverticulum. The surgical measures available, when laparotomy shows this condition is responsible for acute peritonitis, are :—

1. Resection and anastomosis of the segment of jejunum or ileum affected by diverticulosis. Where the distribution is limited and the patient's age and general condition allow a more extended procedure, this operation is the one of choice. When there have been previous symptoms attributable to diverticulosis, the indications are even stronger. The complication of late intestinal fistula, in *Case* 2, might have been avoided by this procedure, though he was at the time of operation judged unfit for it.

2. Excision of the perforated diverticulum is a sound operation, and particularly applicable where diverticulosis affects a considerable length of intestine, or where the condition has not given rise to previous symptoms.

FIG. 94.—The enterolith causing obstruction in *Case* 3. (Approximately natural size.)

3. Invagination of the whole sac into the lumen of the gut is suggested by Ferguson, Krasner, and Cameron (1947) on the grounds that diverticula are subserous protrusions of only mucosa and submucosa, and when so treated will atrophy.

4. Simple suture and patching of the perforation is a quick, surgically satisfactory operation, valuable where the patient's age and general condition require the minimum of operative handling. The two cases described in this paper were treated in this way.

5. Laparotomy and drainage of the peritoneal cavity without any measure directed at repair or excision of the perforation might well be the most that a desperately ill patient with established peritonitis could withstand.

*Case* 3.—Mrs. I. W., aged 61, was admitted on Oct. 5, 1951, with a history of having had epigastric pain for two weeks, associated with retrosternal burning. These were relieved by alkalis. She had no previous history of dyspepsia, nor had she ever been jaundiced. Two days before admission, colicky lower abdominal pain had commenced, with persistent vomiting of small quantities of green fluid. On admission to a medical ward she was found to be in no pain, her temperature 98·4° F., pulse 90. Her abdomen was full, but there was no free fluid and no tenderness or mass was found on palpation. She was diagnosed as suffering from biliary colic and treated conservatively. Her condition remained unchanged during the next twenty-four hours, but she vomited three times on Oct. 7. A surgical opinion was sought on the following day, when she was having recurring attacks of moderately severe abdominal colic. The abdomen was distended, peristaltic sounds being increased and suggestive of obstruction. A pre-operative diagnosis of gall-stone obstruction was made.

OPERATION.—Through a right paramedian incision, the ileum was found to be collapsed; on tracing it proximally, the jejunum was obstructed about 5 ft. from the duodenojejunal flexure by a hard irregular ovoid mass 2 in. by 1½ in. (*Fig.* 94), above which the jejunum was grossly dilated. The impacted mass was removed by enterotomy. The gall-bladder was palpated, but found

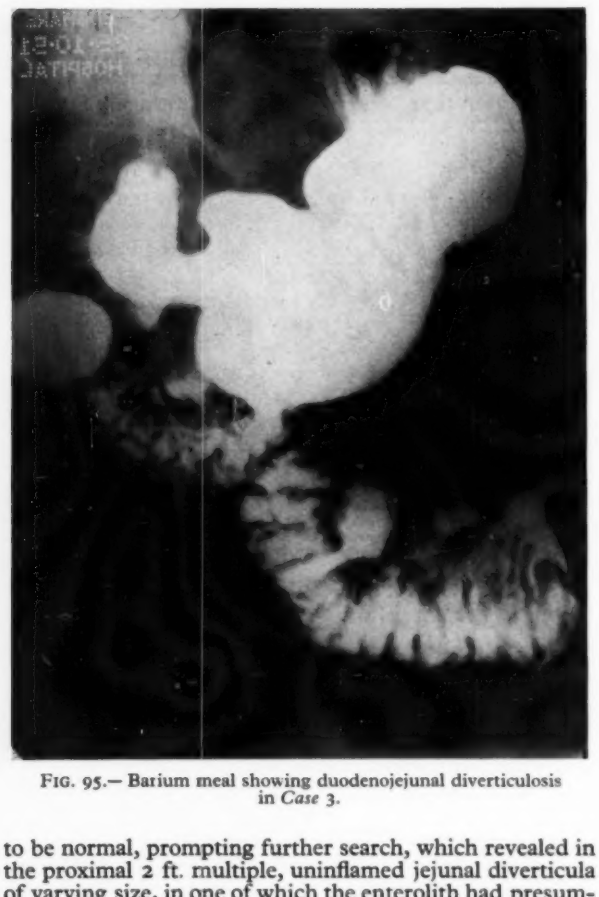

FIG. 95.— Barium meal showing duodenojejunal diverticulosis in *Case* 3.

to be normal, prompting further search, which revealed in the proximal 2 ft. multiple, uninflamed jejunal diverticula of varying size, in one of which the enterolith had presumably arisen.

Following an uneventful convalescence the patient was discharged on Oct. 28. A barium meal showed no evidence of peptic ulceration, and the radiologist, Dr. E. Topham, reported two diverticula arising from the second part of the duodenum, three more from the third part, and at least three, though probably more, from the proximal jejunum. (*Fig.* 95.)

**Discussion.**—Concretion formation in a diverticulum of the small intestine is an uncommon complication, though a number of cases have been recorded. Their presence may lead to further pathological events and Klidjian (1946) describes a case of fairly massive hæmorrhage into the intestine, necessitating excision of the bleeding diverticulum, in which was found an enterolith. I have found no record of jaundice being caused by a duodenal diverticulum containing an enterolith, though this has occurred in the absence of any concretion. In the case reported by Ward-McQuaid and Gordon (1950), though an enterolith was present in a duodenal diverticulum, obstruction of the common bile-duct was due to a carcinoma of the head of the pancreas.

Impaction of a solid mass is a rare cause of intestinal obstruction, the commonest being either a gall-stone or an aggregation of fruit skins. True enteroliths originate either in intestinal diverticula, or in a segment of bowel loculated by stricture formation, local stasis being one important factor in their formation. Richards (1951) describes such a case and refers to 10 others in the literature.

I have been able to find reports of 7 cases where an enterolith, developing in a diverticulum, gave rise to obstruction. Milnes Walker quotes three from the literature, though in only one had the concretion been extruded and become impacted at a point lower in the small intestine. In the two others the concretions had reached such proportions that they filled not only the diverticulum in which they formed, but encroached on the lumen of the jejunum. Hellstrom (1936), Shaw (1941), Goodall (1948), and Armitage, Fowweather, and Johnstone (1950), report cases similar to the case described in this paper. That such impaction may not necessarily lead to acute and progressive obstruction is illustrated by the case described by the last-mentioned authors.

## SUMMARY

The acute complications which may develop in diverticula of the small intestine are briefly reviewed and reference made to the literature on the subject.

Two cases of acute jejunal diverticulitis with perforation are described and mention is made of the operative measures which may be employed.

A case of acute intestinal obstruction by impaction of an enterolith originating in a jejunal diverticulum is added to the cases reported in the literature.

I should like to express my appreciation to Mr. Frank Forty, under whom these cases were admitted, for the encouragement and advice he has given me in making this record, and for allowing me to operate on them.

I am grateful to Miss M. H. Shaw, who is responsible for the photography.

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# NEURILEMMOMA OF BONE

By H. MORUS JONES
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NEURILEMMOMA is a type of nerve-sheath tumour which is known to occur in many parts of the body, principally in the soft tissues, in direct association with peripheral or visceral nerves. It has been referred to by a bewildering variety of names, indicating a difference of opinion as to its origin. Verocay (1908) described a specific form of encapsulated benign tumour of the sheath of peripheral nerves and introduced the term 'neurinoma'. Mallory (Mallory and Parker, 1927) suggested the term 'perineurial fibroblastoma' to indicate an origin from the fibroblast of the nerve-sheath and 'Schwannoma' was suggested by those who thought the tumour arose from the sheath of Schwann. In an attempt to avoid the difficulty over the nomenclature, and since it is generally agreed that this is a tumour of the neurilemma, Masson and Stout introduced the term 'neurilemmoma', which is now in general use (Stout, 1935).

An extensive search of the literature reveals that there are only a few instances of the occurrence of this tumour in bone. De Santa and Burgess (1940) described 2 cases of their own, one occurring in the ulna, the other in the sacrum. They could find only one previous reference to the undoubted occurrence of neurilemmoma in bone—that described by Gross, Bailey, and Jacox (1939). They considered that a further case, occurring in an ulna, described by Peers (1934) as a primary intramedullary neurogenic sarcoma, could also be accepted. A further case occurring in the sacrum was described by Conley and Miller (1942). A brief summary of the main features of the cases described in long bones is given in *Table I*.

## CASE REPORT

Mrs. R. P., aged 44, attended the out-patients' department at Ashford Hospital, Middlesex, on April 4, 1950. She complained of the presence of a swelling on the back of her left hand and was referred to hospital as a case of 'ganglion'.

HISTORY.—In 1946 she had sprained her left hand, and a few days later she had noticed the appearance of a swelling over the region of the head of the fourth metacarpal bone, which had gradually got larger and had recently caused a little pain.

EXAMINATION showed a cystic swelling 2 in. in diameter over the fourth metacarpal bone of the left hand. The swelling could be fluctuated and transilluminated. A drawing is shown in *Fig.* 96.

No other swellings could be detected on clinical examination, and there was nothing to suggest the presence of multiple neurofibromata. X-ray examination showed almost complete destruction of the fourth metacarpal bone. (*Fig.* 97.)

Chondromatous changes were suggested as the most likely cause. Radiography of the chest was clear, and the long bones showed no abnormality.

DIAGNOSIS.—A tentative diagnosis of a chondroma was made and the patient was advised to have it removed. She was accordingly admitted to hospital on April 11, under the care of Mr. E. N. Callum.

TREATMENT.—After suitable skin preparation, operation was carried out on April 15. A dorsal longitudinal incision over the fourth metacarpal was made and a tumour was found which was involving the head and base of the fourth metacarpal. The bone complete with tumour was removed. A bone-graft corresponding to the length of the metacarpal was obtained from the tibia, placed in position and the wound closed.

RESULT.—The patient made a good recovery. Post-operative œdema of the hand and limitaton of movements

FIG. 96.—Drawing of the cystic tumour of the left hand as seen when the patient was admitted for operation.

improved with remedial exercises and encouragement of active movements, and the patient was discharged on April 24. She was last seen in the out-patients' department in September, 1951, when there was good function of the left hand. Radiographs showed periosteal reaction in the third metacarpal and a trace of new bone was visible around the proximal end of the bone-graft replacing the fourth metacarpal (*Fig.* 98).

PATHOLOGICAL REPORT.—

"*Macroscopically*: the tumour measures 6 × 4 × 3 cm., and is divided into two lobes by a shallow groove. The smaller lobe has a smooth surface, the larger exhibits two nodules. Cross-section shows that the nodules are bony for about 3 mm. in depth, but there is no bone deeper. The remainder of the tissue is translucent, with white flecks in it.

"*Microscopically*: the tumour is divided into lobules and these show the palisading of cell nuclei of type A

neurilemmoma, while the intervening strands show the picture of a neurilemmoma type B. (*Fig.* 99.) There is no evidence of malignancy, and I have not previously seen a neurilemmoma in bone."

## DISCUSSION

On clinical and radiological grounds this tumour was thought to be a chondroma. The pathological report, however, and comparison with the previous cases described left no doubt that the tumour conformed with all the characters of a neurilemmoma. These are :—

1. The tumour is of long duration when first seen.
2. The most common and often the only symptom is the physical presence of a tumour.
3. The tumour is always single and circumscribed.
4. The clinical course appears to be benign and local removal appears to be adequate.
5. The tumour is not usually diagnosed clinically but on microscopical examination.
6. Prognosis after local removal appears to be good.

In addition, the case described bears a striking resemblance in anatomical and X-ray appearances to the cases of neurilemmoma previously described in long bones by Gross and others (1939), by Peers (1934), and by De Santa and Burgess (Case 1, 1940).

FIG. 97.—X-ray appearances of the tumour, showing almost complete destruction of the fourth metacarpal and cystic spaces in the bone.

All four involved the mid-shaft region of the bone, and the X-ray appearances of a cystic expansive rarefaction is markedly similar. Local removal and bone-graft produced a good result, as in those described by Gross (1939) and Conley and Miller (1942).

Localization of the tumour in the mid-shaft region may be related to the nerve-supply to bone. Kolliker (1854) gave a description of the anatomical distribution of the nerves in bone, which he observed as

*Table I.*—DETAILS OF NEURILEMMOMA IN LONG BONES

| AUTHOR | SEX | AGE | DURATION AND SYMPTOMS | SITE OF TUMOUR | X-RAY APPEARANCES | PATHOLOGY | TREATMENT | SUBSEQUENT HISTORY |
|---|---|---|---|---|---|---|---|---|
| 1. GROSS, BAILEY, and JACOX (1939) | Female | 37 yr. | 3 years ; painless mass over left upper arm | Mid-shaft of the humerus (L.) | Cystic area in mid-shaft | Soft, solid. Micro : Typical neurilemmoma | Local excision | No record |
| 2. PEERS (1934) | Male | 55 yr. | 1 year : swelling of right forearm | Mid-shaft of the ulna (R.) | In middle third ulna fusiform tumour pushing thin cortex bone before it. Thin bony septa divide tissue into loculi | Whorl-like. Fibroblastic areas with palisading of nuclei | Amputation | Alive 20 months later |
| 3. DE SANTA and BURGESS (1940) | Male | 37 yr. | 8 years ; repeated fractures of left forearm | Mid-shaft of the ulna (R.) | Multilocular cystic change with thin shell of cortical bone | Soft, hæmorrhagic. Micro : Typical neurilemmoma | Resection with bone-graft | No record |

being derived from the periosteum, which was richly supplied, and by one or more fine nerves which accompanied the nutrient artery. Any of the neoplasms arising from peripheral nerve-fibres may, therefore, arise from the nerves in bone and the rarity


## SUMMARY

A case of neurilemmoma arising in a metacarpal bone is described, the origin of the tumour probably being from the nerve-sheaths of the sparse

FIG. 98.—X-ray appearances one month after operation, showing bone-graft in position and some periosteal reaction in the third metacarpal.

of neurilemmoma may be ascribed to the paucity of these fibres.

Although osseous changes may occur in the multiple neurofibromata of von Recklinghausen's

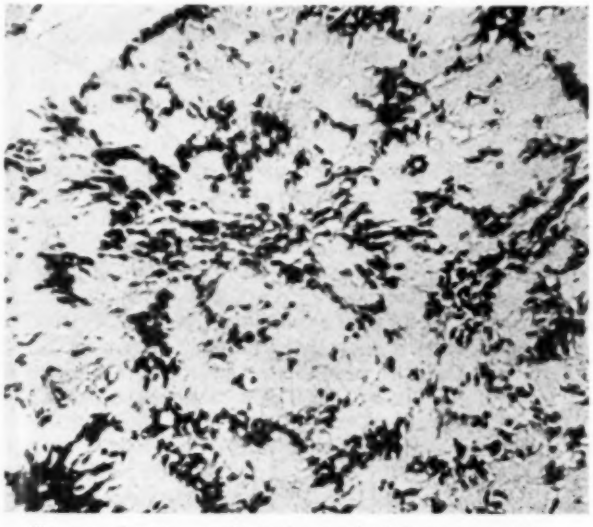

FIG. 99.—Low-power photomicrograph of the tumour, showing palisading of nuclei.

disease, in none of the cases mentioned in this report were stigmata of the disease found, despite a careful search. It is concluded, therefore, that the tumour is not related to the less specific type of neurofibroma found in von Recklinghausen's disease and must not be confused with it.

nerve-trunks within the marrow cavity which accompany the nutrient vessels into the bone. Treatment was by local removal, and insertion of a bone-graft, which appears to have been perfectly adequate. It is emphasized that neurilemmoma may occur as a primary tumour in bone, and that in considering the diagnosis of cystic lesions in the mid-shaft of a long bone the possibility of its being a neurilemmoma should be considered.

My thanks are due to Mr. E. N. Callum for permission to publish this case and for helpful criticism; to Professor W. D. Newcomb for making the pathological diagnosis; to Dr. W. F. Hamilton for the pathological report; also to Dr. C. V. Ross and Mr. E. A. Targett, F.I.M.L.T., for the photomicrograph, and to Miss B. E. Nicholson for the drawing.

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# INTESTINAL OBSTRUCTION DUE TO KNOTTING OF TWO LOOPS OF SMALL INTESTINE

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KNOTTING of the intestine is very rare, but has been described before from time to time and in various countries. Braun (1928), in a table of operative results in intestinal obstruction, described 4 out of his 465 cases as due to intestinal knotting; 3 died and 1 was cured by operation. Details of the nature of the knots are not available. The condition is apparently less uncommon in Scandinavia, and Kallio (1932) described 161 cases collected from the literature. Most of these cases had intertwined loops of intestine, but some of them had true knots. True knotting of the intestine occurs when two loops become crossed (*see Fig.* 105 C) and one of the loops passes through the aperture made by the crossed loops (*see Fig.* 105 E) encircling the base of the other loop. Intertwining refers to the twisting together of two crossed loops of intestine. The case of Nyström (1921), recorded by Kallio, undoubtedly comes under the category of a true knot, but many of his other cases were merely complicated twists, volvulus, or intertwining. Faltin (1937) refers to the cases described by himself, Kallio, and other surgeons in Finland, of intestinal knots, and reviews well over 100 examples from that country. In these cases the ileum was found tied in complicated knots producing intestinal obstruction, but there are very few records of similar conditions in England or America. Frimann-Dahl (1942) described the radiological appearances in cases of intestinal knots, but the two cases he recorded had intertwining of crossed loops of small intestine and sigmoid colon. Paul (1940) described a similar case of intertwining of a loop of small intestine and colon in which operative intervention was followed by recovery.

FIG. 100.—The specimen from its posterior aspect. The cut edge of the mesentery is seen running from above downwards. Normal intestine is held in the hand above. On the lower right side, touched by the fingers of the other hand, is the smaller strangulated loop which was found on the right of the mesentery. To the left is the larger left-sided strangulated loop. Between the strangulated loops is seen the collapsed encircling loop.

FIG. 101.—The specimen from its anterior aspect. The arrow rests on the right strangulated loop and points to the terminal ileum. The left strangulated loop is seen on the right side of the photo and upper ileum above.

From the descriptions given by these authors it seems that intertwining of loops of lower ileum and sigmoid colon are the least uncommon pathological lesions found in cases of intestinal obstruction from intertwined loops. True knotting of a loop consisting of the cæcum, ascending colon, and terminal ileum, and of another loop of ileum occurred in Nyström's case, and cases of so-called knotting of two or three loops of small intestine are described. Some of these probably had true knots, but not only is the exact anatomical relationship of the bowel difficult to understand but a description and diagrammatic representation also present difficulties as the knotting of the bowel and exact part played by the folding of the mesentery lead to obscurity. Cases in which a loop of intestine has passed through an aperture in the mesentery cannot be regarded as examples of knotting.

At autopsy it was difficult to understand what displacement of the intestine had taken place in the present case and only after studying the preserved specimen closely in the laboratory was its nature clearly comprehended.

## CASE REPORT

The patient was a Hindu male, aged 35 years, employed as a servant by a foreman on the Kolar Gold field, South India. There was no relevant previous history.

At 7 p.m. on Nov. 21, 1950, while waiting at table, he felt a sudden severe peri-umbilical abdominal pain. He had to stop work and vomited twice. The pain continued without remissions or exacerbations until 10 p.m. when the patient was admitted to hospital.

FIG. 102.—The encircling loop is held to the left and partially covers the right strangulated loop. The left strangulated loop is on the right side of the photo. Upper intestine is seen above. The aperture can be seen.

ON EXAMINATION.—He was found to be extremely shocked and semi-comatose. Temperature 97° F., pulse 74, respiration 20. The abdomen was a little distended, especially below the umbilicus, and was generally tender. There was no rigidity, but a mild degree of guarding was noted. Liver dullness was present and intestinal sounds were heard.

Owing to the continuous nature of the pain a tentative diagnosis of paralytic ileus was made. This is the commonest form of intestinal obstruction in this district and intestinal sounds are present in a fair percentage of cases (Roantree, 1949). A Ryle's tube was passed and continuous gastric aspiration was commenced. Morphine ¼ g. was given subcutaneously and a continuous drip intravenous half-normal 5 per cent glucose-saline commenced.

From 10 p.m. to 7 a.m. the gastric intake was 195 c.c. and gastric aspirate 480 c.c. He had 3 litres of intravenous half-normal 5 per cent glucose saline during that time and passed 240 c.c. of urine. At 7 a.m. distension had increased, the abdomen was generally rigid, and the pulse had risen from 60–120 per minute. Laparotomy was decided upon, the diagnoses considered being: (1) Perforated typhoid ulcer; (2) Mechanical intestinal obstruction with strangulation; (3) Non-mechanical intestinal obstruction.

During incision of the parietes the patient developed peripheral circulatory failure; it was deemed unwise to proceed and the incision was closed. Death took place at 2·10 p.m., 19 hours and 10 minutes after onset.

AT AUTOPSY.—This was started at 5 p.m. There were about three pints of sanguineous fluid in the peritoneal cavity and strangulated coils of small intestine, black and distended with blood, came into view. The strangulated coils were situated in the lower ileum and a volvulus of that part of the gut was first considered, but was soon excluded. As the exact mechanism of the strangulation was not easily determined, the lesion was removed *in toto* by tying and dividing the terminal ileum, cutting the mesentery at its line of attachment to the posterior abdominal wall, and dividing the upper ileum well away from the strangulated portion. After some examination and thought it was discovered that two loops of small intestine had become tied tightly in a knot, producing two strangulated loops, one to the right and one to the left of a constricting band consisting of a length of intestine and mesentery encircling the portions of small intestine involved.

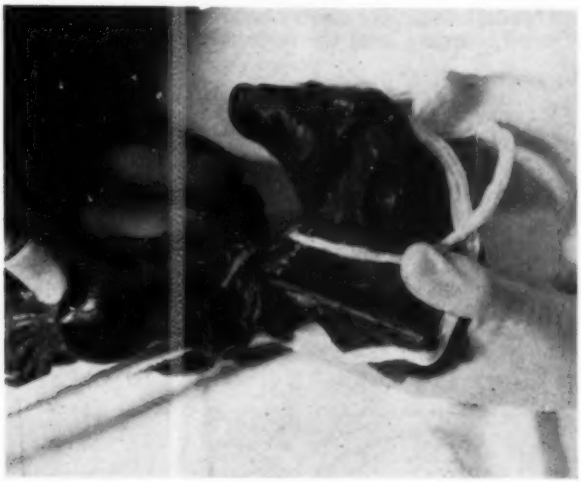

FIG. 103.—The larger left strangulated loop is held to the right of the photo with the hand and tape. The right strangulated loop, encircling loop, and upper ileum is held to the left of the photo.

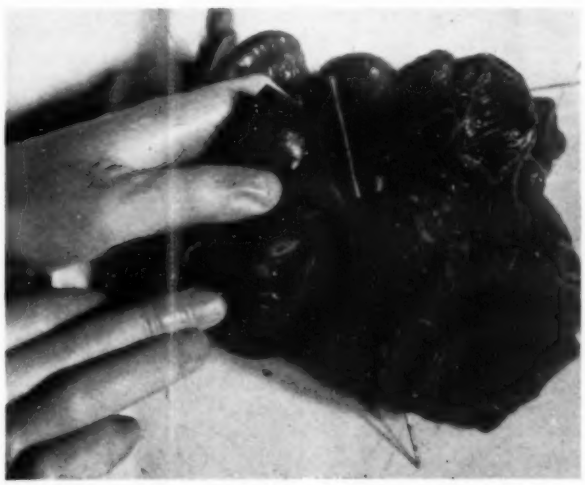

FIG. 104.—The smaller right strangulated loop is held in the right hand. A probe passes through the aperture. The collapsed encircling loop partially covers the left strangulated loop. Normal intestine is seen above.

*Figs.* 100–104 are photographs of the specimen after five days in 10 per cent formalin. *Fig.* 105 is diagrams showing the process of knotting and the final result.

*Fig.* 106 is a diagrammatic representation of the relationships of the gut drawn during examination of

the specimen, and *Fig.* 107 is a similar diagram depicting the gut and mesentery. It will be seen that the anatomical relationships are similar in *Figs.* 105 F and 107.

*Fig.* 108 is a photograph of a piece of knotted rope demonstrating the presence of the same anatomical relationships as those in the specimen of intestine and may help the understanding of *Fig.* 107.

A description dictated while examining the specimen was as follows: The specimen consists of several feet of small intestine from the terminal ileum upwards, with its mesentery divided at the line of attachment to the posterior abdominal wall. There appears to be an aperture in the mesentery 3 in. from the ileocæcal junction and 1 in. from the mesenteric border of the intestine. At first sight it seems that loops of intestine have prolapsed through an aperture in both directions. The upper intestine is normal. On following this intestine downwards it becomes discoloured and somewhat distended 2 ft. before it passes through the aperture from right to left.

It passes through this apparent aperture adjacent to the ileocæcal junction and through another leaf of mesentery so closely attached to the aperture that it seems continuous with it (it was later discovered that this configuration was caused by a portion of mesentery folded back on itself, the convex border forming the edge of the aperture). The intestine can next be identified on the left side of the mesentery, where it forms a strangulated loop 3 ft. long. Passing back through the aperture

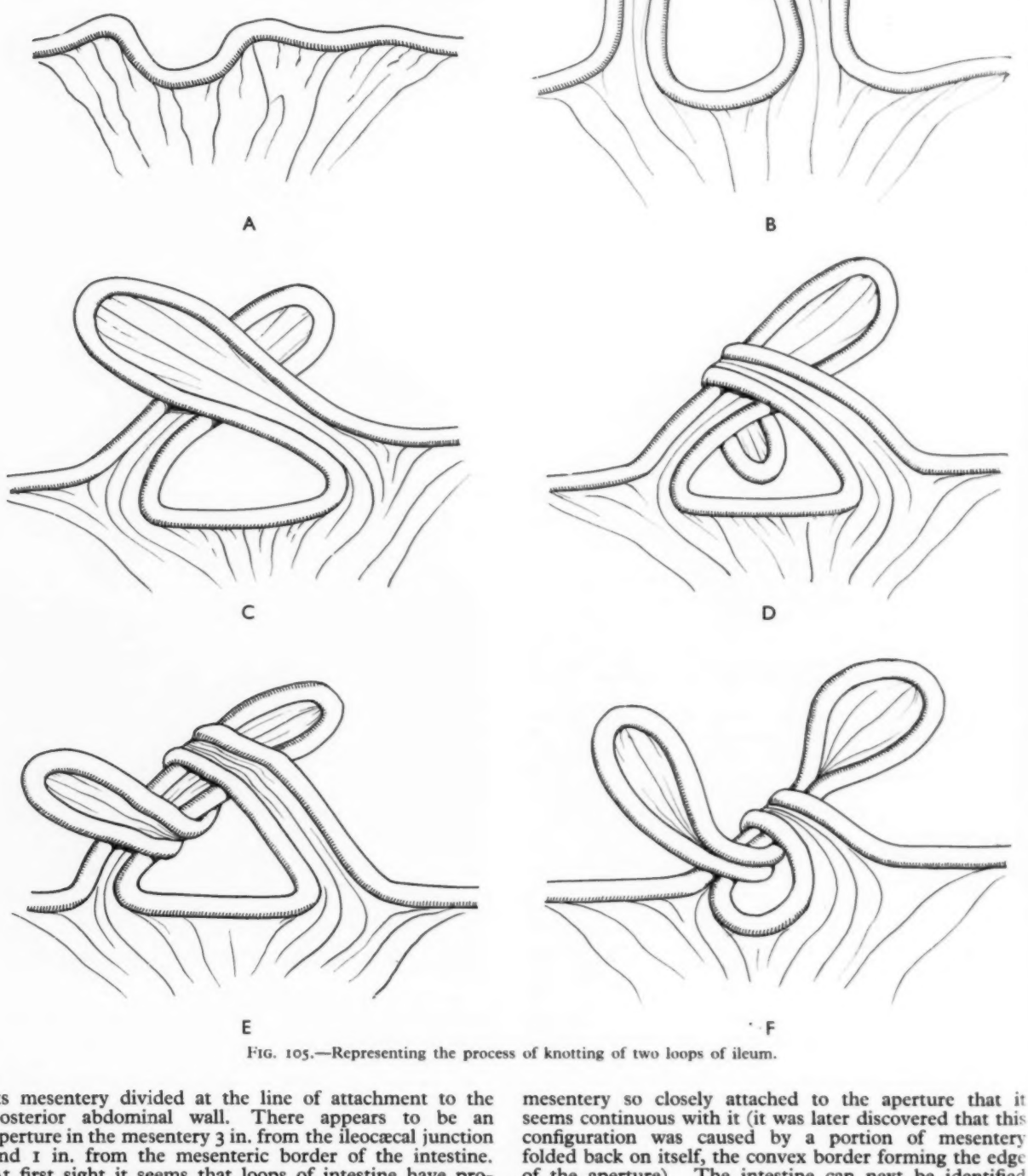


FIG. 105.—Representing the process of knotting of two loops of ileum.

to the right side, the intestine next passes right round the aperture again, joins the left side, passes through the aperture from left to right and forms a strangulated loop 1 ft. long on the right side. All portions of intestine are exceedingly constricted where they pass through the aperture. The distal end of the last-mentioned loop passes back through the aperture again, and is seen on the left-hand side tightly around the aperture as the terminal 3 in. of ileum.

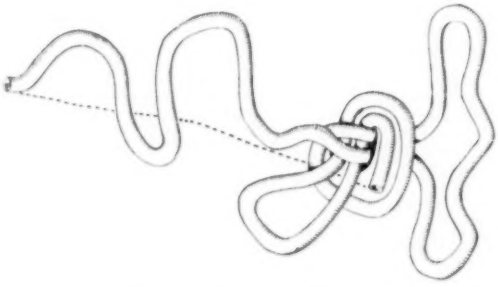

FIG. 106.—Diagram of specimen drawn during examination.

## DISCUSSION

**Mechanism.**—Volvulus of organs tends to occur when the mesentery is unduly long, when the organ is pathologically adherent to other structures, and, in the case of intestine, when there is unusual length, chronic distension, or when the mesentery is narrow at the base of a loop. The same factors would predispose to intestinal knotting, and in this case the presence of loops of small intestine with abnormally long mesenteries, narrow at the bases of the loops, must be accepted. There were no adhesions, no remnants of the vitello-intestinal duct were present, nor were there any signs of chronic pathological lesions in the bowel. It seems likely that a combination of abnormal factors would be necessary to produce this rare pathological condition, and one possibility is that besides an abnormally long mesentery the intestine was weighted with unusual contents, e.g., the loops may have contained semi-solid contents. This occasionally happens in this district where the diet consists of rice, millet, or maize, is bulky, and is sometimes taken in an unappetizing, cold, conglomerated mass.

It seems almost inconceivable that even if two loops of intestine were long enough to become knotted, and if by unusual intestinal movements they came to lie in a knotted position, that they would not immediately slip back into normal relationships. Nevertheless the knot did occur and was not spontaneously reduced. Instead it tightened. Once this commenced and there was intestinal obstruction with vascular occlusion the loops inevitably became congested and distended with fluid and gas, with resultant tightening of the knot to a degree at which all blood-supply was cut off, the intestine and mesentery encircled being tightly constricted. Death occurred rapidly from loss of effective blood-volume due to hæmorrhage into the long length of bowel affected.

**Diagnosis.**—A surgeon confronted with knotting of the intestine during laparotomy for intestinal obstruction would have great difficulty in deciding on the exact nature of the lesion, unless alive to the possibility of intestinal knotting. With this form of intestinal strangulation in mind he would have no difficulty in recognizing the condition once he saw a strangulated loop protruding on either side of an encircling loop.

**Treatment.**—The best course to pursue on recognition of intestinal knotting would depend on the tightness of the constriction and therefore on the

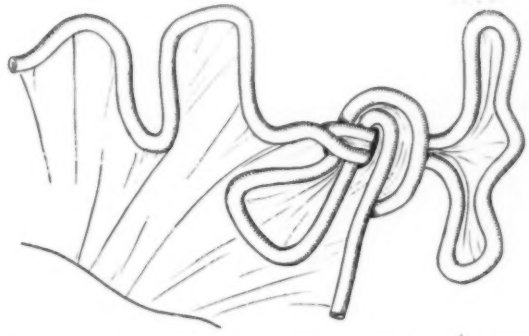

FIG. 107.—Diagram of specimen with mesenteric attachments shown.

degree of strangulation and viability of the intestine. Possible procedures would be :—

1. Undoing the knot.
2. Undoing the knot after aspiration of contents of intestinal loops.
3. Resection of one loop, undoing the knot (which would be easy after resection of one loop) and assessment of further procedure.

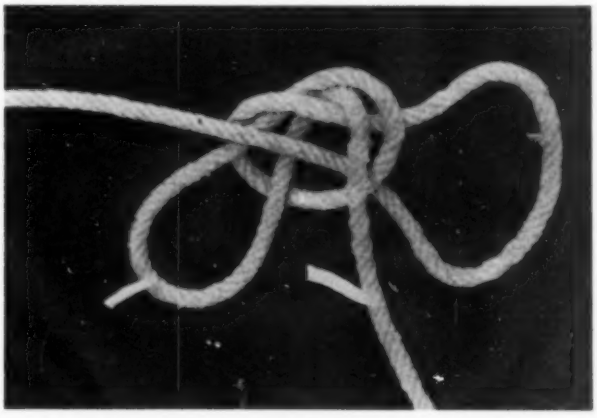

FIG. 108.—A piece of rope with two loops knotted together for comparison with the previous diagrams.

4. Resection of whole knot and non-viable intestine.
5. Exteriorization and enterostomy.

In the case under discussion (1) and (2) would have been impossible as the knot was so tight. The third would have been the only course to adopt offering a reasonable chance of recovery, but even after undoing the knot further extensive resection would have been necessary. In addition the constriction was so intense that the four portions of intestine passed through an aperture less than an inch in diameter. At the sites of constriction it is almost certain that a ring of intestine would have

been non-viable. Apart from this consideration the right-hand loop (1 ft.) and the left-hand loop (3 ft.) and 2 ft. of ileum proximal to the constriction were black and doubtless non-viable.

Method (4), the simplest procedure possible in the circumstances, and the least likely to lead to contamination, would have been a formidable procedure in such a shocked patient and as 7–8 ft. of small intestine were involved the probability of a fatal result would have been great. (5) Exteriorization and drainage of the ileum before it reached the knot and drainage of the strangulated loops, if combined with adequate transfusion of blood, might have tided the patient over until his condition warranted further major procedures, but it is unlikely that he would have improved sufficiently with a high enterostomy in existence.

It seems that when dealing with a case of intestinal knotting if attempts at undoing the knot fail even after aspiration of loops with syringe and needle, the best procedure would be resection of the whole knot with end-to-end anastomosis through healthy intestine.


## SUMMARY

A case of acute intestinal obstruction and strangulation due to knotting of two loops of ileum is described. The mechanism of knotting, diagnosis during laparotomy, and possible lines of treatment are discussed.


I have pleasure in thanking Dr. W. B. Roantree, Chief Medical Officer, Kolar Gold Field, for his kind help in preparing this article, and I wish to thank the Managers, Messrs. John Taylor & Sons (India) Ltd., Oorgaum, for permission for publication.

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# GAS CYSTS OF THE INTESTINE


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ONLY 200 cases of this rare condition have been recorded in the literature since Bang (1876) was credited with describing the first case of cystic pneumatosis in a human subject. There had been previous descriptions of somewhat similar conditions in swine. Nitch (1924) showed that gas cysts were frequently associated with gastric or duodenal ulcer, and stated that 83 per cent of these cases were complicated by stenosis. Since this time Pybus (1934), Berglund (1939), and recently Somerville (1951) have reported a similar association.

In the case now recorded the gas cysts formed bands, leading to attacks of small-intestinal obstruction which masked the symptoms of developing pyloric stenosis. None of the previously reported cases have noted the tendency to band formation by gas cysts, although Gasin, Brooke, Lerner, and Price (1949) and Nitch (1924) reported cases where obstruction was associated with pneumatosis.

## CASE REPORT

The patient, a man aged 56, had periodic attacks of abdominal pain following a left strangulated hernia in 1944. The pain was of a colicky nature and occurred frequently following this period. It was relieved by vomiting and the vomitus had a foul smell. He was admitted on Sept. 21, 1948, for observation. His appetite had been getting poorer and he had been gradually losing weight. His abdomen was distended, and, as the pain was of a colicky nature associated with vomiting, a diagnosis of intermittent obstruction was made. At the first operation on Oct. 7 the abdomen was explored through a right paramedian incision. The small intestine was distended and showed a finely white reticulated mosaic appearance, and at one point there were gas cysts of varying dimensions, giving a soap-sud effect. A large omental band was found to be encircling the mesentery, and this band was divided. The cæcum was noted to be extremely mobile, and it was considered that this might well be the cause of a recurrent volvulus. In view of the fact that Jones (1948) had reported a volvulus to be present in his case, it was thought advisable to fix the cæcum. This was done by appendicostomy, bringing out the appendix through a small stab incision in the right iliac fossa. The wound was then closed in layers. He made a satisfactory recovery from this operation and seemed to be greatly improved, being discharged from hospital on Oct. 19.

He was again admitted on Dec. 30. He had been free from pain until three days prior to admission. On that date crampy abdominal pain began and was associated with vomiting. The pain was sub-umbilical in position, and the onset of the pain had been followed by abdominal distension. A diagnosis of recurrent obstruction was made and on Dec. 30 operation was again performed. The old incision was opened and an area of gas cysts in the intestine was found about 6 in. long, involving two pieces of adherent gut. The first photograph of the condition was taken at this time, and is shown in *Fig.* 109. It was noted that the bowel proximal to the band, as demonstrated, was distended. The band was divided, and an opportunity was taken to undo the appendicostomy as it was apparent that the mobile cæcum could not be the cause of the condition. It was interesting to observe how the appendix had elongated. Although the appendix had been pulled through the wound at the first operation and the cæcum drawn close to the anterior abdominal wall at the time of the second operation, the intraperitoneal portion was 3-4 in. in length. The patient made a satisfactory post-operative recovery, being discharged from hospital on Jan. 6, 1949. He was kept under review and seemed much improved for about six months. At this time, however, he was still having a little colicky pain, but was feeling much better and was fit to work. On Aug. 28 he was seen again, and as the

pain was persisting it was decided to admit him for a barium meal and 'follow-through'. He was not admitted until Jan. 23, 1950, by which time he had developed further attacks of vomiting. The vomitus consisted of large quantities of greenish coloured fluid. His pain had now become upper abdominal and was

FIG. 109.—Band formation associated with gas cysts of the intestine producing intestinal obstruction.

relieved by vomiting. There was no real history, however, of indigestion.

A barium meal was performed, and this revealed an almost complete pyloric stenosis. *Fig.* 110 shows the degree of gastric residue after six hours, which Dr. D. Ramage reported upon as a very definite pyloric stenosis. At the same time an opportunity was taken to X-ray the subdiaphragmatic region as gas had been noted under the diaphragm by Sloan (1920), Pybus (1934), Gasin and others (1949), and Somerville (1951). *Fig.* 111 shows

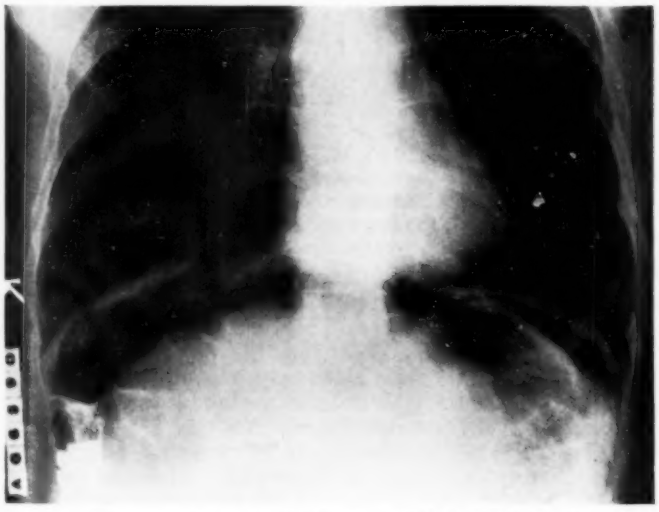

FIG. 111.—Gas under diaphragm. To the left side definite mottling may be seen. These are undoubtedly cysts on the intestinal wall.

gas under the diaphragm, probably due to ruptured cysts causing free gas in the abdominal cavity. In the absence of perforation of the bowel or artificial pneumoperitoneum, this radiological finding was considered by Gasin and Somerville to be diagnostic of gas cysts in the intestine. The third operation was performed on Jan. 31, an upper midline abdominal incision being used. At this operation a loop of small intestine, which is shown in *Fig.* 112, was found lying between the diaphragm and liver, and it is probable, therefore, that the gas shown in *Fig.* 111 was this loop of bowel. Indeed,

FIG. 110.—Six-hour residue in stomach following barium meal, showing associated pyloric stenosis with gas cysts of the intestine.

to the left side of the radiograph it is possible to see the mottling which is produced by multiple gas cysts. This appearance was also noted by Gasin and others. *Fig.*

FIG. 112.—Demonstrating loop of bowel found lying between liver and diaphragm.

113 shows the obvious pyloric stenosis which was present. The distended stomach can be clearly seen, and between the operator's right finger and thumb a very narrow pylorus is observed. Posterior gastro-enterostomy was performed. No attempt was made to deal with the gas cysts, but it was noted that there were elongated tags arising from the cystic area, and undoubtedly it was these

tags which, becoming adherent, had given rise to obstruction at the previous operations. There was, however, no obstruction observed on this occasion. Some of the material was removed for pathological examination. The patient made a satisfactory recovery from this operation, and was discharged home on Feb. 14.

The histological report on the specimen by the late Dr. K. D. Hunter stated: "This specimen showed numerous cystic spaces of varying size lined for the most part by a single layer of flattened cells. Surrounding the cystic spaces there is loose connective tissue containing many blood-vessels. Dense fibrous tissue is seen in some areas. The band shows similar appearances consisting of loose connective tissue containing thin-walled blood-vessels and lymphatics. The appearances are compatible with diagnosis of cystic pneumatosis."

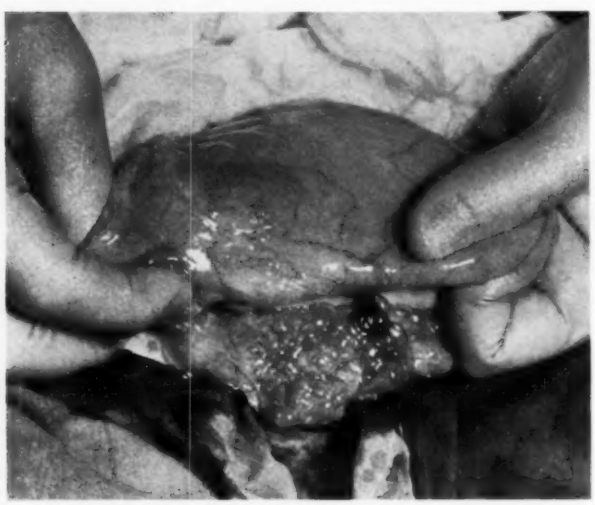

FIG. 113.—Pyloric stenosis is clearly demonstrated with dilatation of the stomach.

## COMMENT

The aetiology of gas cysts has been the subject of much discussion. Neoplastic and infective theories have been postulated. It would appear, however, that the mechanical theory has received most support in recent times. This theory suggests that gas is forced out through a mucosal defect by excessive intestinal peristalsis. There is, however, no experimental evidence to support this mechanical theory. A fresh post-mortem specimen of bowel was obtained and two small incisions made in the mucosa. The whole preparation was then distended with air at 65 mm. Hg for a period of twenty-four hours, drying of the bowel being prevented by submerging the preparation in a saline bath and covering the exposed loops with damp cotton-wool. In relationship to one incision a few small bubbles appeared in the subserosal area, but the experiment was not conclusive.

Illingworth and Dick (1947) state that pneumatosis does not give rise to symptoms of clinical importance. It is felt that the case-history and operative findings in this patient belie their statement. The complications which may be produced by this condition are well shown in *Fig.* 109. No other reported case has, however, produced obstruction. Treatment of the associated lesion appears to cure the condition. Mori (1907), Jackson (1940), and Berglund (1939) all had opportunities to reopen the abdomen after treatment of the primary condition. It was found that the gas cysts had disappeared.

## SUMMARY

1. A case of gas cysts in the intestine is reported.

2. Complications arising from this condition are described. There is a tendency to band formation which may produce obstruction.

3. The presence of associated pyloric stenosis was demonstrated in this case as in others, the treatment of which would appear to have produced a cure of the pneumatosis.

4. It is considered possible that the escape of gas into the subserosal tissues is mechanical, peristalsis producing a similar effect to emphysema elsewhere. This supposition was tested but remains unproved.

I would like to acknowledge the radiographs produced by the Department of Radiography, Royal Victoria Infirmary, Newcastle upon Tyne, and the photographs produced by the Department of Photography, King's College, University of Durham.

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# STRANGULATION IN A DIAPHRAGMATIC HERNIA FROM INDIRECT VIOLENCE

By R. ABBEY SMITH and S. SARKISSIAN

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PERUSAL of the literature suggests that acute strangulation of small bowel proceeding to gangrene in diaphragmatic herniæ due to indirect violence is rare. This may be because the majority of such herniæ are repaired before strangulation occurs or that the isolated case is not published. However, the small intestine is one of the less frequent of the viscera to strangulate through a torn diaphragm, and references to such an event are rare.

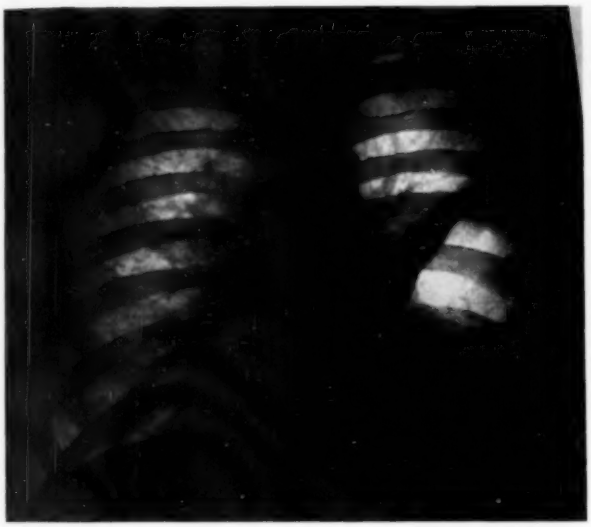


FIG. 114.—Radiograph of chest two days after accident.

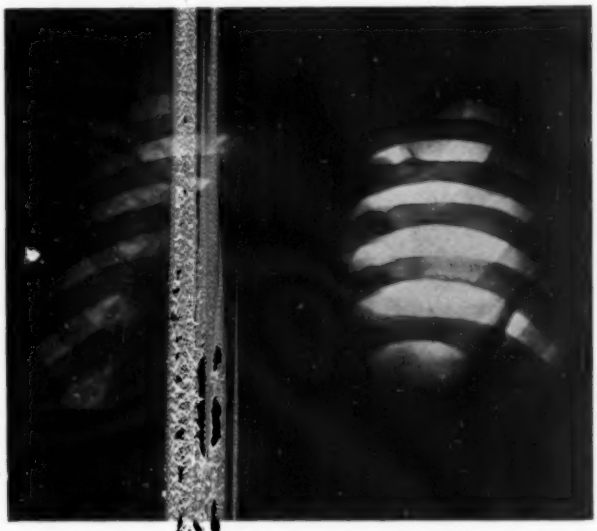


FIG. 115.—Radiograph of chest at time of admission to the Thoracic Unit at Warwick.

Carter and Giuseffi (1948) reviewed 39 cases of strangulated diaphragmatic hernia, of which 8 were due to indirect violence of one form or another to the lower thorax or upper abdomen. Well-recognized causes are severe crushes, falls, or automobile accidents. Of these 8 herniæ, only 3 contained small bowel. All were left-sided, no sac was present in any, and in none of these three cases was the small intestine the only viscera incarcerated.

In a complete review of diaphragmatic hernia, Morton (1939) writes: "often times the symptoms of traumatic herniations are masked by the shock", and, again, "in other accidents the herniation symptoms are completely submerged". The authors of the paper previously quoted (Carter and Giuseffi, 1948) observe that strangulation may be atypical in symptoms. The case description which follows confirms these views of the traumatic hernia from indirect violence. The mode of onset and progress of symptoms in this case were made no less perplexing by the straightforward statement of the patient that he was suffering from a diaphragmatic hernia, for which he had declined operation.

## CASE REPORT

HISTORY.—A male commercial traveller, aged 28, of robust mental and physical constitution, was six months previously involved in a motor-car accident. He suffered, apart from minor abrasions, a hard blow on the upper abdomen from the steering wheel of his car and was admitted to a local hospital. A radiograph of the chest (*Fig.* 114) two days after the accident demonstrated a rupture of the left dome of the diaphragm with visceral herniation, by barium meal examination shown to be the greater portion of the stomach. He had no symptoms from this and was known to have had a normal X-ray appearance of his chest four years previously. Some two weeks following his accident he was transferred to the Thoracic Unit at the General Infirmary at Leeds and was seen by Mr. R. Allison, who advised immediate admission for operative repair of the hernia. For pressing business reasons the patient refused this advice and, symptom-free, proceeded on his way. During the succeeding six months he continued his normal life without notable symptoms.

The day before he was seen by us he set out on a car journey. After three hours' driving he was conscious of a discomfort in the left chest beneath the nipple. He could not recall any straining or minor exertion to precipitate this upset. Within five minutes of its onset he was obliged to get out of his car to "walk off" the pain, and within three-quarters of an hour it had become an intense, continuous, boring pain over the whole of the left chest. Its severity was overwhelming and so violent was the patient's reaction to the pain that he was considered to be in a maniacal state, and was given large doses of narcotics. He was transferred to our care twenty hours after the commencement of the pain.

ON ADMISSION.—Although obviously extremely ill, the patient was sitting up in bed reading the evening newspaper when first seen in the ward. He indicated that the pain had eased considerably and was able to give a concise report on his previous barium meal examination and the nature of the hernia. There had been no nausea or vomiting throughout. The patient had moved his bowels normally shortly before admission and flatus had been passed freely up to the time of his admission.

He was dyspnœic, the respiration grunting, and cyanosis of the lips was present. The pulse-rate was 150/min. and

impalpable at the wrist. The temperature was subnormal. No systolic blood-pressure could be recorded. He was euphoric and seemed oblivious of his somewhat precarious state.

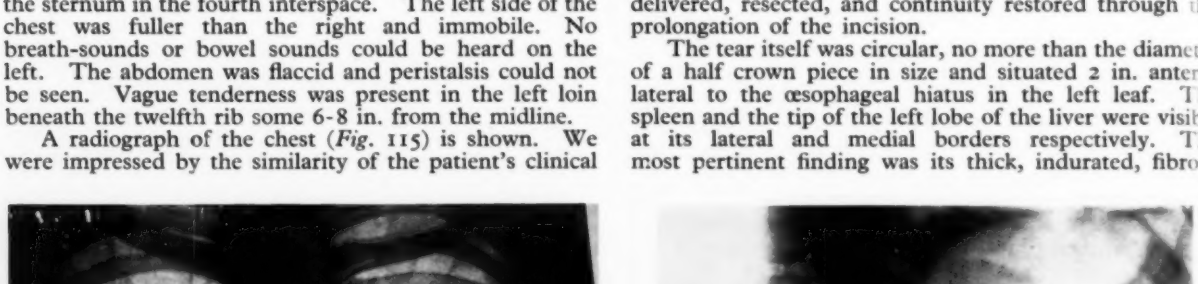
The apex beat of the heart was 1 in. to the right of the sternum in the fourth interspace. The left side of the chest was fuller than the right and immobile. No breath-sounds or bowel sounds could be heard on the left. The abdomen was flaccid and peristalsis could not be seen. Vague tenderness was present in the left loin beneath the twelfth rib some 6-8 in. from the midline.

A radiograph of the chest (*Fig.* 115) is shown. We were impressed by the similarity of the patient's clinical state and radiograph with cases of tension pneumothorax we had previously encountered. To avoid a harmful operation for a valvular pneumothorax complicating a diaphragmatic hernia, it was decided to aspirate the left pleural cavity. It should be noted that only this film (*Fig.* 115), was in our possession at the time. Aspiration of the left pleural cavity was carried out, cautiously and with diffidence, through the first interspace in front. A blunt induction needle was used. No positive pressure from the left chest could be obtained and no fluid aspirated.

Further ancillary means of diagnosis were considered undesirable. The patient made no response to oxygen by B.L.B. mask and transfusion over three hours. In the continued absence of the signs of intestinal obstruction, a diagnosis of perforation of a gastric ulcer into the pleural cavity was made and operation undertaken.

OPERATION (24 hours after onset of pain).—Pentothal, curare, gas and oxygen anæsthesia supplemented by 1 per cent novocain block of 6-10 left intercostals inclusive. The seventh left rib was resected and the pleural cavity opened. About 15 oz. of blood-stained fluid were present. There was no air. No hernial sac covered the bowel in the chest. A gratifying improvement in the patient's condition was noted as soon as the mediastinum returned to a more normal position as the bowel herniated into the wound. The whole of the stomach, the transverse colon and splenic flexure, portions of the great omentum, and about 4 ft. of distended small bowel were returned to the abdomen without difficulty by enlarging the tear in the left leaf of the diaphragm. Firmly held by a band was a further length of gangrenous small bowel. The band was divided and the bowel was released. At the point of constriction the bowel was near to rupture, and the whole length was black. The shortness of its mesentery prevented any attempt at resection from above; accordingly the diaphragm was incised, the costal margin divided, and the abdominal cavity entered. The length of bowel—32 in. of mid-jejunum—was delivered, resected, and continuity restored through the prolongation of the incision.

The tear itself was circular, no more than the diameter of a half crown piece in size and situated 2 in. anterolateral to the œsophageal hiatus in the left leaf. The spleen and the tip of the left lobe of the liver were visible at its lateral and medial borders respectively. The most pertinent finding was its thick, indurated, fibrous rim, undoubtedly the result of a natural attempt to heal the tear and not a characteristic of the congenital diaphragmatic deficiencies.



A B

FIG. 116—Radiograph of chest and barium meal examination ten weeks after operation.

The diaphragm, from hernial ring to costal margin, was closed with sixteen No. 20 thread sutures, the phrenic nerve crushed, and a drain inserted into the pleural cavity. The lung, which had been atelectatic and invisible in the upper thorax, expanded without difficulty. The chest wall was closed.

PROGRESS.—The patient progressed without untoward incident. He was discharged from hospital at the third week.

Six months later he was well, symptomless, and working. The left hemidiaphragm was higher than the right and moving paradoxically. There was no recurrence of the hernia. His plain radiograph (*Fig.* 116 A) and barium meal (*Fig.* 116 B) are shown.

## SUMMARY

1. A case of strangulation of stomach, transverse colon, and small bowel through a tear in the left leaf of the diaphragm from indirect violence is recorded.

2. The case supports the view that strangulation may be atypical in its symptoms and the signs thereof confusing.

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# MULTIPLE RETICULOSARCOMA OF THE DUODENUM AND JEJUNUM

By J. G. C. SPENCER

FROM THE DEPARTMENT OF PATHOLOGY, UNIVERSITY OF BRISTOL

THE small intestine appears to be one of the least frequent sites of malignant disease in the whole body, and Hoffman and Pack (1937) estimate the incidence as 0·03 per cent of all autopsies. These authors also consider that only 0·3 per cent of all gastro-intestinal neoplasms are found in the small bowel, whereas Ewing (1940) puts the figure at 3·0 per cent and Raiford (1932) at 4·9 per cent. The jejunum, in spite of its length, is less subject to this form of disease than either the duodenum or the ileum. In the case recorded here, 32 tumours were found in the jejunum and one in the third part of the duodenum.

## CASE REPORT

HISTORY.—The patient was a man of 37 who was in good health until he presented himself at hospital on Dec. 22, 1950, with a four-week history of gastric flatulence and a feeling of abdominal distension. These symptoms were unrelated to food and examination revealed no abnormal physical signs. However, in view of his repeated vomiting, a barium meal and gastroscopy were carried out, but again the findings were normal and he was discharged to out-patients for observation. Six weeks later he was re-admitted to the Bristol Royal Infirmary under Mr. Cooke on account of worsening symptoms, epigastric pain, and anorexia.

AT OPERATION.—At laparotomy multiple intussusceptions were at once apparent throughout the jejunum,

FIG. 117.—Three segments of the jejunum opened to display some of the tumours.

re-forming as soon as they were reduced, and it was possible to make out the presence of solid lesions of the bowel. No actual perforation of the gut was then present; but in view of the widespread distribution of the lesions further operative procedure was abandoned and the patient died three days later, six and a half weeks after his first attendance at hospital.

AT AUTOPSY.—The jejunum throughout its length showed thirty-two sessile or pedunculated tumours varying from 0·2 × 0·3 cm. to 7·0 × 3·0 × 1·0 cm., projecting into the lumen of the bowel, for the most part situated on or near the antimesenteric border (*Fig.* 117). This situation is at least suggestive of their origin from the lymphoid follicles which are mostly found in the antimesenteric part of the gut. The larger tumours were the site of intussusception, and early perforation of the mucosa opposite a tumour was found in one place. The base of most of the tumours was highly vascular but the peritoneal surface was not destroyed. The

FIG. 118.—Low-power view of a pedunculated tumour, showing the relation of the tumour to the intestinal musculature. (× 3·5.)

third part of the duodenum showed a semi-pedunculated tumour 1 cm. in diameter. The ileum, the appendix, and the large intestine were completely free from tumour or polyp. The mesenteric and regional lymph-nodes were not involved and the sole demonstrable metastasis was a nodule 0·8 cm. in diameter situated in the lower lobe of the left lung, where it had produced no macroscopical reaction or disturbance.

HISTOLOGY.—The tumours seem to arise from the submucous layer of the intestine immediately deep to the muscularis mucosæ (*Fig.* 118), the point of origin noted by Corner and Fairbank (1905), invading rather than infiltrating the surrounding tissues. The cells are arranged in regular solid masses bordered by connective-tissue strands that are slender in places and relatively abundant in others (*Figs.* 119, 120). There is only a moderate vascular supply to the intestinal tumours, but in the pulmonary metastasis there is a profuse development of blood-vessels throughout the mass. In no place is there any hint of acinar formation, and the cells appear to be free from melanin or argentaffin pigment and none show any mucin production. The lightly staining nuclei with occasional nucleoli and frequent mitoses show some peripheral condensation against the clearly cut nuclear membrane (*Fig.* 119). These features, together with the irregular, finely granular cytoplasm that stains well with eosin, are characteristic of the primitive reticulum cell. The reticulin pattern is variable: profuse in some areas and almost non-existant elsewhere. Lymphocytes, plasma cells, and a scattering of giant cells are found among the otherwise predominantly reticulum cells, giving a picture such as is found in reticulosarcoma of the polymorphic or mixed type which Robb-Smith (1938) has found not uncommonly in the lymphoid tissue of the intestine. The small metastasis in the lung shows considerable pleomorphism with regard to both size and shape of cell. Bizarre giant cells with a more foamy cytoplasm, and nuclei that tend to be distributed around

the margin of the cell, are even more common than in the primary tumours of the bowel (*Fig.* 121). As in the intestinal lesions, there is a consistent failure to demonstrate mucin production, melanin, or argentaffin pigment.

## DISCUSSION

The multifocal origin of tumours of lymphoid tissue is stressed by Willis (1948) and also by Runnells (1946) in regard to animal pathology where these tumours are more in evidence. Raiford (1932), in his series of small intestine tumours from the Johns Hopkins Hospital, finds that 6 out of 21, or 29 per cent, of those of mesenchymal origin are multiple, no less than ten tumours being recorded in one instance. The subjects are usually young, with an average age of 32 in that series and 33 in the series reported by Ullman and Abeshouse (1932). Males are undoubtedly afflicted more commonly than females: 3 to 1 according to Corner and Fairbank (1905), and 5 to 2 on the reckoning of Ullman and Abeshouse (1932).

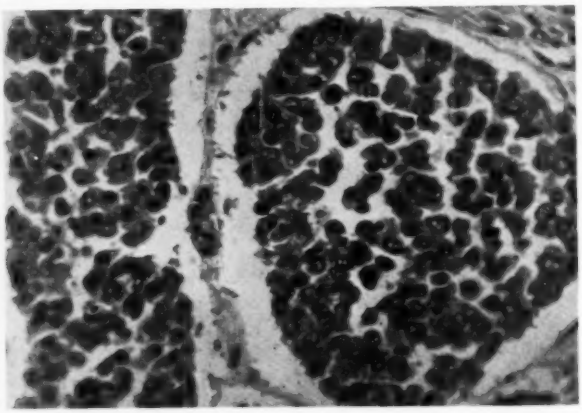

FIG. 119.—A compact part of one of the tumours showing slender connective-tissue strands and many mitoses in the reticulum cells. (× 200.)

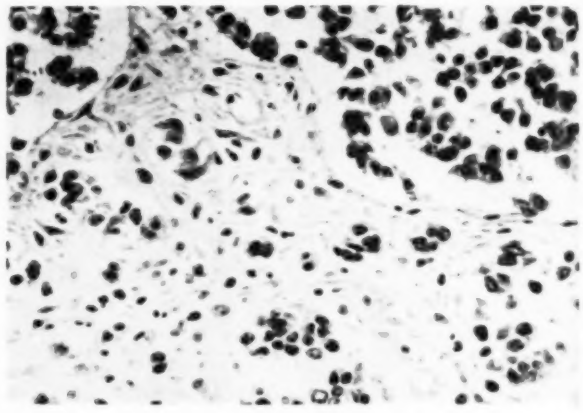

FIG. 120.—Another part of the same tumour showing looser texture, and a scattering of plasma cells, lymphocytes, and giant cells. (× 200.)

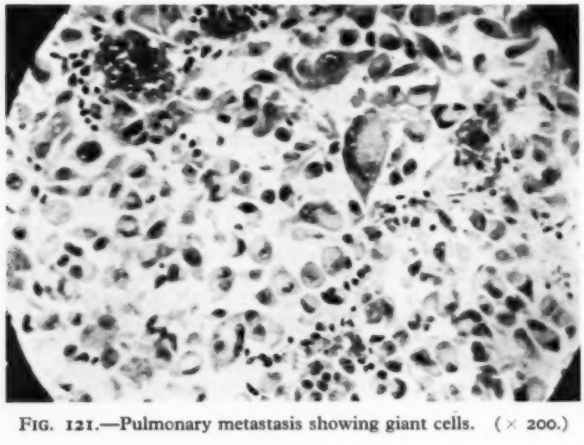

FIG. 121.—Pulmonary metastasis showing giant cells. (× 200.)

The degree of development of lymphoid tissue in the small intestine and spleen contrasts sharply with the infrequency of primary tumours in these sites, though Corner and Fairbank (1905) regard the ileum as one of the sites of election for lymphoid neoplasia. This observation is confirmed by Robb-Smith (1938) and by Ewing (1940). Raiford (1932) and Cohn, Landy, and Richter (1939) find that lymphoblastoma or reticulosarcoma are more frequent than either carcinoma or carcinoid in the small intestine, and it is surprising to find that remarkably little attention has been paid to these tumours in the literature, which Ewing (1940) rightly describes as chaotic. The confusion of which Ewing and Ullman and Abeshouse complain probably resides in the difficulty that surrounded the subject before Robb-Smith's (1938) description and classification of reticulosarcomata became available. Consequently these tumours have to be distinguished from Hodgkin's disease, lymphoid granuloma, Crohn's regional ileitis, leukæmia, or even from melanoma. There can be little doubt that a fairly large proportion of the cases collected into the earlier series includes some belonging to these categories. These intestinal tumours are described under various headings, of which lymphosarcoma, lymphocytoma, and lymphoblastoma are the most frequent, though it still does not follow that every case so described should be assumed to be a reticulosarcoma. Crowther (1913) collected 122 cases and Graves (1919) 246, adding a further 3 of his own. Ullman and Abeshouse (1932) found 126 new cases including 1 case of their own, and incorporated them into a comprehensive review of the subject, but Raiford's (1932) smaller collection is probably the more valuable in virtue of the fullness of the pathological detail available.

Most growths of the small intestine present with obstructive signs and are seldom diagnosed before operation; 30 per cent, according to Raiford (1932), show intussusception, but on the whole he finds that malignant tumours tend to be non-obstructive. Ullman and Abeshouse (1932) noted that intussusception is sometimes seen, but for the most part in the polypoid variants, as in the case reported here. The relative infrequency of their visible metastases tends to jeopardize the proper estimation of the malignant propensities of the reticulosarcomata as opposed to the carcinomata, which by comparison are slow to metastasize. Where local conditions permit, resection of a suitable length of bowel and mesentery seems to offer a fair outlook when followed by

radiotherapy. On the other hand, Ullman and Abeshouse (1932) consider that every case of lymphoid malignant tumour is accompanied by metastases, local or general, by the time operation is reached and consequently they give a much more gloomy prognosis.

## SUMMARY

A case of multiple reticulosarcoma of the jejunum and duodenum is described.

A comparatively brief history was followed by obstructive signs which resulted from multiple intussusceptions throughout the length of the jejunum.

The histological picture of the intestinal lesions and of a single pulmonary metastasis distinguishes the condition from carcinoma, carcinoid, and melanoma.

The literature is briefly reviewed.

I am indebted to Mr. R. V. Cooke for permission to publish this case, to Professor Hewer for much help in preparation of the material, and to Mr. Rogers for the photography.

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# PREVASCULAR FEMORAL HERNIA

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ALTHOUGH probably not exceedingly rare, only 5 cases of this type of hernia have been described in the English and American literature. Of these, the first two were discovered by Stanley during dissection of cadavers and were reported in Teale's book published in 1846. The third was described by Moschocowitz (1912) and this was the first case to be studied *in vivo* and treated surgically. The fourth and fifth were described by Keynes (1932), and these also were treated by operation. The condition was mentioned in Watson's book on hernia published in 1924, in which it is stated that the hernia is probably more frequent than is generally supposed. This opinion was also held by Moschocowitz. In the foreign literature the condition has been described by Fabricus (1895), Narath (1899) (6 cases occurring in conjunction with congenital dislocation of the hip and assumed to be of traumatic origin), Zinner (1915) (post-mortem specimen), Cevario (1921), Desbonnets (1934), Lazurenbo (1935), Aievoli (1935), Santoro (1937), Cuscianna (1938), and Iadevaia (1940).

The purpose of this short communication is to add a further case treated surgically to those already recorded and to discuss briefly the salient points of surgical interest.

**Definition.**—A prevascular femoral hernia is a hernia the sac of which is situated within the femoral sheath and in front of the femoral vessels. Only when the neck of the sac extends laterally across the front of the iliac and femoral vessels should the hernia be designated prevascular. The hernia in which the neck traverses the femoral canal and the sac of which then deviates laterally across the femoral vessels is a femoral hernia with lateral deviation of the sac and not a prevascular hernia.

## CASE REPORT

Mr. C. J. H., aged 68, was first admitted to Clatterbridge General Hospital on July 17, 1950, suffering from acute retention of urine due to prostatic hypertrophy. He also had a large right femoral hernia which was easily reducible. A modified type of Wilson Hey prostatectomy was performed the same day and he was discharged home on Aug. 16 micturating normally and with no symptoms.

On Nov. 6 the patient was re-admitted for repair of his right femoral hernia, as this was causing him considerable discomfort. At that time it was noted that the hernia, although below the inguinal ligament and lateral to the pubic spine, was much larger than the average type of femoral hernia and appeared to spread out in a lateral direction in a quite unusual manner. The second operation was performed on Nov. 8 through a right inguinal incision. After opening the external oblique the neck of the sac was displayed and opened. It proved to be very wide, elliptical in shape, and easily accommodated four fingers placed side by side. It extended from the free edge of Gimbernat's ligament to about 1 in. lateral to the femoral artery. The inferior epigastric artery had been displaced laterally and was divided to facilitate mobilization of the sac. The fundus of the sac projected downwards some 3 in. below the inguinal ligament, and after it had been withdrawn from behind the ligament a clean exposure of the upper third of the femoral vessels was produced, as in Moschocowitz's case. The sac was excised and the neck closed with a running suture. Repair of the large defect was then effected in the following manner : three interrupted nylon sutures were placed at intervals of 1 cm. through the iliopectineal ligament (Cooper's ligament), extending from close to the pubic spine laterally to the femoral vein. The upper and lower ends of these sutures were then passed respectively through conjoint tendon and the inguinal ligament. The three sutures were then securely tied. This had the effect of tightening the conjoint tendon and the very lax inguinal ligament

snugly round the iliac vessels and so effectively blocking the path for recurrence of the hernia. In order to strengthen the rather attenuated inguinal ligament a strip of the pectineus muscle fascia was then raised from the muscle medial to the vessels, carried across in front of the vessels, and stitched at a point 1 in. lateral to the external iliac artery to the inguinal ligament in front and to the psoas fascia behind. Care was taken to avoid damage to the femoral nerve whilst placing the sutures through the psoas fascia. The operation was completed by a relief incision in the deep layer of the rectus sheath and closure of the external oblique without tension. The patient made an uneventful recovery from this operation—the sutures were removed on the ninth day, he was allowed up on the tenth day, and discharged home on the fifteenth day. He was last seen on Jan. 21, 1951, nine weeks after the operation, and the repair seemed perfectly sound.

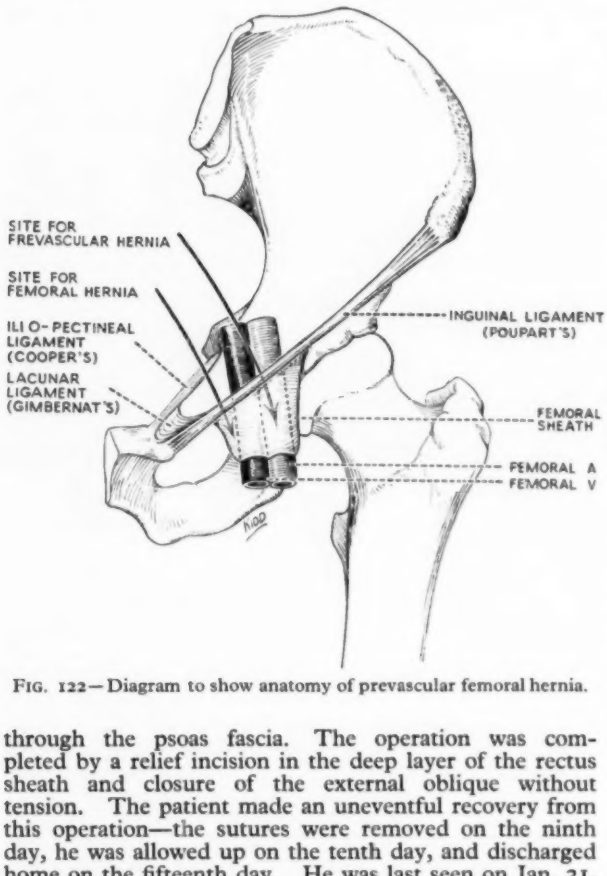


FIG. 122—Diagram to show anatomy of prevascular femoral hernia.

## DISCUSSION

Moschocowitz (1912) pointed out that the prevascular hernia is one in which the hernial sac bursts its way into the femoral sheath as compared with the straightforward femoral hernia which bursts its way into the femoral canal (*Fig.* 122). In these cases it may be assumed that the prolongation of the transversalis fascia onto the anterior aspect of the femoral vessels to form the anterior wall of the sheath is weak, thus allowing the peritoneal hernial sac to burst through. Having once done this the inguinal ligament soon stretches in front of the descending sac and the hernia rapidly increases in size. The relationship of the deep epigastric artery to this form of hernia appears to depend upon how the hernia commences. If it commences as a simple femoral hernia the neck of which later spreads laterally across the femoral vessels, the epigastric artery will be pushed outwards by the sac and lie lateral to the neck. On the other hand, if the hernia is prevascular from its commencement it pushes its way beneath the inguinal ligament, in front of the femoral vessels, and lateral to the epigastric artery, which in this case lies medial to the neck.

**Prevascular Femoral Hernia.**—The question of whether this type of hernia was congenital or acquired was discussed by Keynes in 1932 when he reported his two cases. One of these was assumed to be congenital because the fundus of the sac was wider than the neck, and the other was considered to be acquired because the sac formed a triangular pouch with its base upwards.

As regards treatment, Claud C. Burton, in his collective review of herniæ of the supravesical, inguinal, and lateral pelvic fossæ (July, 1950) states that any hernia emerging through the space between the inguinal and iliopectineal ligaments may be referred to collectively as an interligamentous hernia, and this constitutes an absolute criterion for the three-dimensional or combined inguinopectineal repair. Thus in order to repair these herniæ adequately it is necessary to suture the conjoint tendon to the iliopectineal ligament of Cooper. When the suturing reaches laterally as far as the femoral vein the plane of suturing then moves forwards, and the conjoint tendon is sutured to the inguinal ligament. It is is an advantage to tighten the inguinal ligament around the vessels by taking the medial aspect of this ligament in addition to the conjoint tendon down to the iliopectineal ligament. Even after this it is sometimes necessary, as in the case reported here, to strengthen the inguinal ligament as it passes in front of the vessels. This can be done by raising a flap of the pectineus fascia, carrying it across in front of the vessels and suturing it, lateral to the vessels, to the inguinal ligament in front and to the iliopsoas fascia behind.

I would like to thank Mr. James Moroney and Mr. David Wilkie for their helpful criticism, and Mr. James Moroney for permission to publish this case.

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# A CASE OF TRUE HERMAPHRODITISM

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THE presence in one human gonad of seminiferous tubules and Graafian follicles, both well differentiated, is not unknown but is of sufficient rarity to deserve recording.

## CASE REPORT

HISTORY.—N. S., a daughter of an Arab father and African mother (Kinyamwezi tribe), was born at Tabora after a normal single pregnancy and brought up as a girl. She came to the Government hospital in that town in January, 1951, when she was 17 years old, because her external genitalia were abnormal. There was no family history of anything similar. She was, with some difficulty, persuaded to submit to surgical treatment.

ON EXAMINATION.—In general appearance, distribution of the hair, condition of the breasts, and in the quality of the voice she was a healthy, well-developed young woman. She said that all her instincts were feminine, that she had menstruated every four weeks since she was 14, and that she now wished to marry, but wanted first to be made as much like a normal woman as possible. Only the genitalia were abnormal. Instead of a clitoris there was a well-developed penis, symmetrical and in size like that of a boy of 10 years old, though somewhat bound down on its ventral aspect and with complete hypospadias, the urethra opening at a central orifice in the middle of the perineum. This central orifice was 4 cm. from the anus and was 5 mm. in diameter. At it opened both the urethra and a small vagina, which was not quite large enough to admit an ordinary lead pencil. The left labium majus was normal. The skin of the right was loose, thick, and corrugated like a scrotum and contained a small but well-formed and well-descended testis. This was quite mobile and could easily be pushed up into the inguinal canal, but there was no inguinal hernia.

AT OPERATION (Jan. 26).—The small penis was dissected down to the bifurcation of its crura and cut across with closure of the skin over its base. The loose skin of the right labium majus was cut away with an elliptical incision and the ovario-testis and its coverings removed after division of what can only be described as a spermatic cord. The narrow vagina was dilated up until a little finger could be inserted, and it was then possible to feel at its upper end a small, ill-defined mass which was presumed to represent the uterus.

Healing was uncomplicated. The vagina was dilated at weekly intervals, and when she left hospital it would admit an index finger. Menstruation occurred three months after operation and again at 4-weekly intervals after that, the loss being scanty and always associated with pain. Attempts at intercourse were made but were unsatisfactory and, a year after operation, she was still unmarried.

THE SPECIMENS.—These consisted of a penis-like organ (*Fig.* 123) and a gonad with an associated tube lying within a peritoneum-lined sac (*Fig.* 124), which was opened along one side. The penis-like organ was gently curved along its whole length, and was ovoid in cross-section, measuring 4·5 cm. in length and 1·7 cm. and 1·2 cm. respectively in the longest and shortest diameters at the base. There was a well-defined glans with distinct corona, a prepuce rolled back at the base and a well-developed frenulum. A vertical groove 0·9 cm. long ran from the tip of the glans into the attachment of the frenulum (*Fig.* 123 B). No channel or groove representing the penile urethra could be found in the shaft of the organ. Two corpora cavernosa with distinct capsules meeting medially in a fibrous septum could be seen on the cut surface, but no corpus spongiosum was present. Two pairs of vessels ran in the position of the dorsal vessels of the normal penis, two arteries superficially each accompanied by a nerve and two veins more deeply placed. Microscopically (*Fig.* 125) the erectile tissue of the corpora cavernosa was of typical structure with abundant smooth muscle, but nothing representing either the corpus spongiosum or urethra was found.

FIG. 123.—The penis; A, side view; B, end view. (× ⅔.)

The gonad, a flattened pear-shaped organ, measuring 3 cm. in length, 1·7 cm. wide, and 1·3 cm. deep in its thickest part, was covered with a serous layer which, around its site of attachment above and posteriorly, became continuous with the wall of an open sac resembling a tunica vaginalis. A vascular bundle coursed in the wall of this sac from above and entered the gonad through its attachment to the sac.

Superficially the arrangement was that of testis and tunica vaginalis, but no epididymis or vas deferens could be found either macroscopically or microscopically. The vascular bundle consisted of two arterial channels and a pampiniform plexus of veins. On the outer side of the gonad and attached to the sac wall by a short mesentery was a tube, 1·7 cm. long, the lower end of which had a fimbriated opening into the sac, the whole looking like the outer end of a normal Fallopian tube. In section this was found to be lined with ciliated columnar epithelium and to possess a smooth muscle wall. Above it ended blindly.

Microscopical examination of the gonad revealed that at the lower end the structure was undoubtedly testicular, with obvious seminiferous tubules (*Figs.* 126, 127), although the amount of intervening connective tissue was somewhat greater than in the normal adult testis. The tunica albuginea was well developed and the flattened cells of the tunica vaginalis could barely be recognized as a separate layer, as in the normal adult testis. The tubules resembled those in cryptorchidism, no secondary spermatocytes, spermatids, or mature spermatozoa being seen: indeed, most of the lining cells seemed to be Sertoli cells. In places the tubules were less developed than elsewhere, the lumina being smaller and the lining cells more closely packed and darkly staining. In the intertubular connective tissue there was a preponderance of large granular polyhedral cells like the interstitial cells of Leydig. No efferent ducts, vasa recta, or rete testis were seen. This appearance was seen in the caudal two-thirds of the organ; the cranial third showed an equally convincing ovarian appearance (*Figs.* 128, 129). The covering epithelium here was distinct and cuboidal; cortex and medulla were well differentiated. In the cortex were follicles in different stages of development and degeneration, primordial follicles, mature Graafian follicles, and a number of atretic follicles. The whole of this part of the organ resembled closely the normal ovary of a woman of reproductive age.

FIG. 124.—The 'ovario-testis' and Fallopian tube. (× ⅓.)

FIG. 125.—Transverse section of the penis. (× 4.)

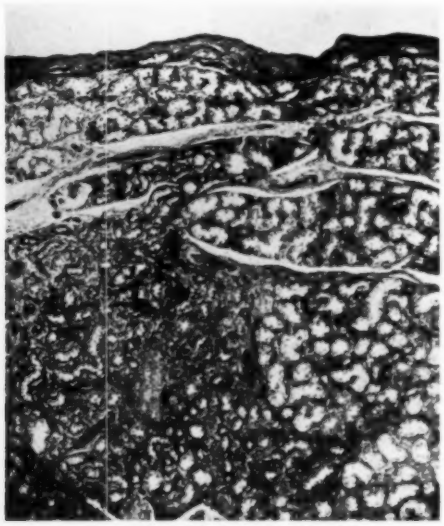

FIG. 126.—Testicular tissue. (× 25.)

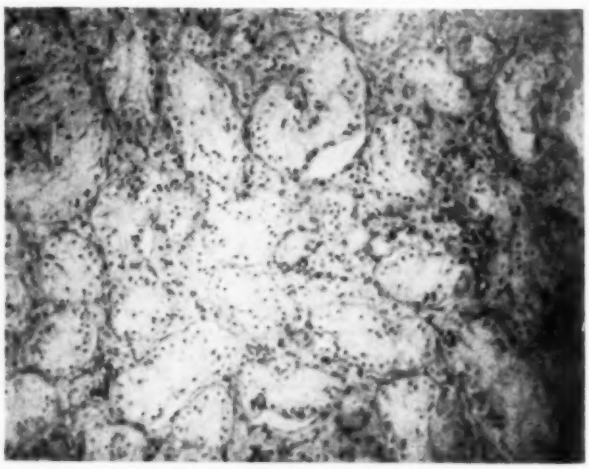

FIG. 127.—Testicular tissue. (× 94.)

## DISCUSSION

This is clearly a case of true hermaphroditism with the presence of an ovario-testis on one side. The condition of the opposite gonad or gonads was undetermined, but in the presence of regular

menstruation after operation one must assume the existence of a uterus and functional ovarian tissue. It is impossible to decide whether the remaining gonad was purely ovarian in nature or another ovario-testis or both ovary and testis separate from one another. This is therefore a case of unilateral or bilateral hermaphroditismus verus.

This condition, though rare, is by now well recognized both in man and animals. In a recent account by Capon (1951) it is stated that 40 authenticated cases have been published. Our case adds a further one to this series. Of these cases 11 were bilateral, 14 unilateral (7 with ovary and 7 with testis on the side opposite the ovario-testis), 11 were heterolateral (ovary and testis on opposite sides), and 4 had an ovario-testis on one side, the nature of the opposite gonad not being determined (Wied, Segaloff, Wiener, and Douglas, 1947). Our case belongs to the last-named category.

Much experimental work has been done on the mechanism of the differentiation of sex in the vertebrates, especially in the cold-blooded vertebrates and in birds. Work on the mammals has not been so great, although Burns (1939, 1942) has made notable contributions in connexion with the marsupials. Two main factors enter into the problem, a genetic and primary factor, and a secondary hormonal influence. The latter has attracted considerable attention since the description by Lillie (1917) of the condition of freemartin in dizygotic cattle twins of opposite sex, where the female calf is influenced by the embryonic hormones of the male and is in consequence hermaphrodite. The genetic constitution controls the sex of the embryo. Sex hormones can only stimulate or suppress organs

FIG. 128.—Ovarian tissue. (× 6.)

already present. All embryos at one stage in development possess both male and female structures such as the Wolffian and Müllerian ducts. Their suppression or further development is under the control of the sex hormones. The literature on human hermaphrodites contains but few references to the family history: this is surprising in view of the association with twinning in cattle. Wied and others (1947) have described a case in one of twins, both siblings however being female. In view of the interstitial implantation of the human chorionic vesicle, as opposed to the superficial in cattle, early fusion of the chorionic vascular trees in dizygotic human twins would probably occur less frequently and the development of a freemartin in the human is less likely to occur than it is in cattle.

As Young (1937) points out, the libido and emotions of the hermaphrodite are conditioned by the manner of upbringing of the individual. In many cases there is an inguinal hernia associated with the genital abnormality, the sac not only containing a gonad but in some cases part or the whole

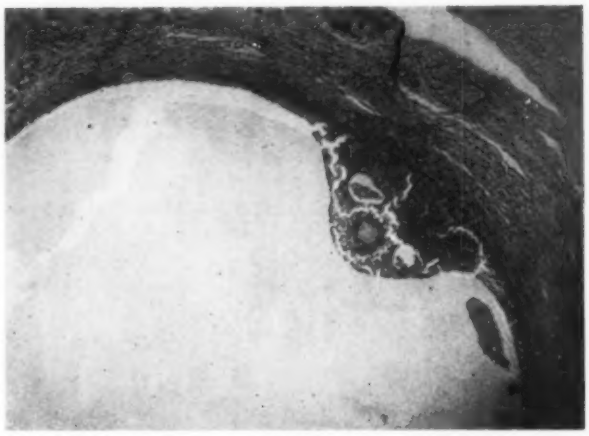

FIG. 129.—Ovarian tissue. (× 60.)

of the uterus, as in the cases by Meyer (1925) and Young (1937). The phallus is always enlarged, even when all external parts are otherwise female in form, and there is frequently some degree of hypospadias. In most cases the breasts enlarge at puberty and tend towards the female type, as do the external contours of the individual. On the other hand, the voice generally deepens at puberty despite these other decidedly feminine traits. This is in accordance with the observations that androgens have but slight effect on mammary tissues, and it is likewise suspected that the œstrogens have little part to play in the control of the growth of the larynx. Of the internal organs of generation the uterus and vagina are present in all cases which have been adequately examined but frequently show abnormalities, such as atresia of one horn of the uterus or of the vagina, a bicornuate condition of the uterus, absence of a Fallopian tube, or frequently opening of the vagina into the proximal part of the urethra and not to the exterior. When these organs are normal in form they are always hypoplastic, the vaginal canal being narrow and the uterus small. The onset of menstruation is delayed, but its rhythm and duration are often normal although the loss at each period may be small.

Records of the male internal organs of generation do not appear to be so complete. The presence of a prostate is described in a few cases but it is uncommon. It is difficult to be certain about the seminal vesicles as they do not appear to have been recorded: if they do occur it must be very rare. Their late development, in the fourth month according to Frazer (1931) or somewhat earlier according to Hamilton, Boyd, and Mossman (1945), renders their appearance subject to the influence of the already acting sex hormones. The vasa deferentia and epididymis are variously developed.

The problem of hermaphroditism still presents many unsolved aspects. The precise nature and mode of action of the 'embryonic' sex hormones needs further elucidation and their role in human development in particular is not yet fully settled.

## SUMMARY

1. The history is given of a case of true hermaphroditism.

2. The anatomical findings are described in detail.

3. This case adds one to a series of some 40 comparable cases previously recorded.

4. The relation to hermaphroditism in animals is discussed, as are some aspects of the mechanism by which this condition may be produced.

5. An outline is given of the anatomy of recorded cases of human hermaphroditism.

Acknowledgements are due to the Director of Medical Services, Tanganyika, for permission to record this case, and to Mr. A. L. Woodling, St. Thomas's Hospital Medical School, for the photographs.

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# FAT EMBOLISM

## WITH A REPORT OF 9 CASES

BY A. J. ALLDRED, OSWESTRY

THE introduction of the antibiotics has removed most of the danger of severe infection from the treatment of fractures. Other complications such as non-union are better understood and can be dealt with effectively by improved techniques in fixation and bone-grafting. Fat embolism, although it has interested surgeons for nearly a century, is still not well understood. It must be regarded to-day as one of the commonest and most serious complications of a fracture.

British interest in the subject was stimulated by the experience of surgeons in the last war, and comprehensive reviews of the subject have been made by Watson (1937), Robb-Smith (1941), Wilson and Salisbury (1944), and Newman (1948). All have sought to show that fat embolism is a common and easily recognizable condition. None has claimed a full understanding of the pathology.

## INCIDENCE

Fat emboli are frequently found in the lungs at post-mortem in a wide variety of conditions, e.g., Catsaras (1920) reported 18 per cent of 67 patients dying from post-influenzal pneumonia. Vance (1931) reported that 20 per cent of the patients he examined at post-mortem with fractures of the long bones showed severe fat embolism. Wilson and Salisbury reported 8 cases with clinical fat embolism, of which 6 were fatal, in 1000 battle casualties, including 119 cases with fractures of long bones.

It would seem from these figures that fat embolism is more common than is generally realized and that the less severe cases are frequently not recognized as such. With this in mind, cases of fractures of long bones with unexplained symptoms such as a sudden rise in temperature which could possibly be attributed to fat embolism have been examined and of 12 suspects 7 have been found to have sufficient physical signs to support the diagnosis. Included in this series are 2 cases who died at adjacent hospitals.

## SYMPTOMS

These usually commence between thirty-six and forty-eight hours after the fracture, but may occur within the first twenty-four hours. An analysis of 24 cases, including 7 reported by Newman (1948), 8 by Wilson and Salisbury (1944), and the 9 in this series, shows that 20 of them presented symptoms within forty-eight hours. In view of this the writer feels that Speed's (1916) often-quoted axiom of " third hour shock, third day fat embolism, third week pulmonary embolism " would be more accurate if it read " second hour shock, second day fat embolism, second week pulmonary embolism ".

The first striking symptom is a change in the patient's general condition accompanied by a rise in temperature. This may be sudden or progressive over several minutes. The patient becomes restless, often with pain in the chest and slight dyspnœa. If seen at this stage, he will be found to be cyanosed and uneasy, with a raised pulse-rate and a normal blood-pressure. During the subsequent few minutes cerebral symptoms begin to manifest themselves. The extent of the changes produced in the central nervous system seems to bear a close relationship to the amount of fat released into the general circulation. If the patient is struck by sudden and deep coma, this implies that large quantities of fat have been released and the prognosis is very grave. If, however, the patient shows merely drowsiness or is irrational, his chances of survival are good, as this indicates a smaller release of fat with less involvement of the brain.

A most striking symptom is the development of incontinence of urine in a patient who has previously enjoyed good health and who has had no urinary

symptoms. In 6 of the 9 cases in this series incontinence was noted and in 2 no record was kept. One other was catheterized on admission and died from his embolism within twenty-four hours. Thomas has also been impressed by this symptom and it is felt that it has not been sufficiently stressed in previous articles. Any young patient with a fracture who develops sudden incontinence about the second or third day should be suspected of having fat embolism.

The temperature chart will show a rise to between 101° and 103°. Higher temperatures may be seen

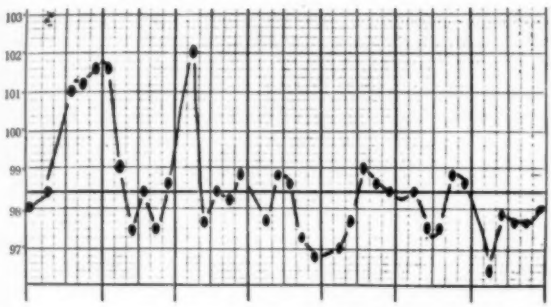

FIG. 130.– *Case* 6. Showing the typical temperature chart from a case of fat embolism.

in cases with severe embolism where the temperature-regulating centre has been involved. A typical example is seen in *Fig.* 130, which shows the chart of *Case* 6 of this series which recovered. Surgeons are familiar with this type of chart, which is often seen after fractures. It is felt that some of these cases which have no clinical evidence of infection severe enough to produce such a fever are instances of fat embolism of minor degree. It is suggested that if all cases of fracture showing a temperature on the second day had a thorough clinical examination of the skin and central nervous system, physical signs confirming the diagnosis would be found in many.

## PHYSICAL SIGNS

These are found in the skin and conjunctiva, the chest, and the central nervous system.

**1. Skin and Conjunctiva.**—Fat embolism produces a most striking petechial rash. It is most frequently seen over the upper chest, the neck, and shoulders, but may be seen in the conjunctiva. In this series it was seen in the neck or chest in 6 cases and in the conjunctiva in 1 case. It is said to occur occasionally on the arms and the rest of the trunk.

The number of petechiæ vary from a few to several hundreds. They differ in size and number to the square inch. They are brightest when they first appear and fade within the first two days, but remain visible for several days and finally disappear except for small areas of pigmentation representing the bigger ones. A characteristic example is seen in *Fig.* 131, taken the morning after it developed in *Case* 6.

**2. The Chest.**—In almost all cases physical signs can be found in the chest. These consist of moist sounds with patchy areas of consolidation. The patient may cough up an increased amount of sputum, but this is not blood-stained.

**3. The Central Nervous System.**—Here are found the most important signs which often clinch the diagnosis by the evidence of a widespread condition of the brain.

*a. Cortical Signs.*—There may be restlessness or a change in personality going on to drowsiness or frank coma. In *Case* 7 the condition precipitated several attacks of petit mal which disappeared within six weeks. The incontinence may be due to cortical involvement or to damage to lower centres.

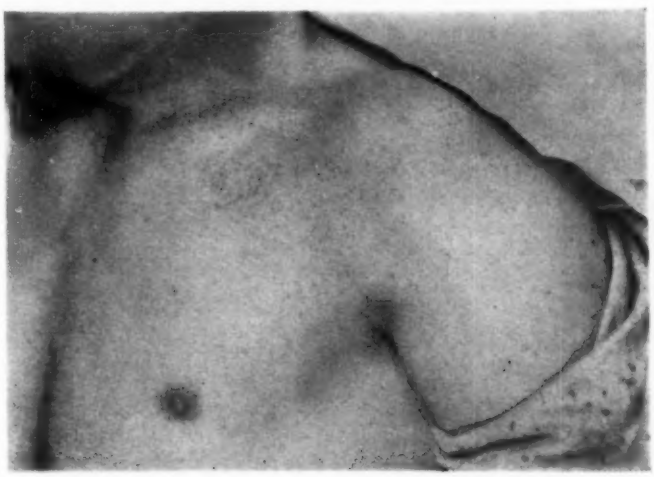

FIG. 131.– *Case* 6. Showing the petechial rash of fat embolism distributed over the upper chest, neck, and shoulders.

*b. Internal Capsule.*—This is characterized by spasticity of the limbs as in *Case* 3 or hemiplegia as in *Case* 4.

*c. Midbrain.*—Changes in the pupils, such as inequality or failure to react to light, as in *Case* 3, may be seen.

*d. Brain-stem.*—It is suggested that emboli may affect the temperature-regulating centre and cause the sudden rise in temperature. Petechiæ are frequently seen in the brain-stem at post-mortem.

In the milder cases the physical signs may be transient and disappear within twelve hours, e.g., *Case* 5, which had an extensor plantar response that disappeared twelve hours later.

## SPECIAL TESTS

These may be used to help in the diagnosis, but in this series were found to be of less importance than the symptoms and signs.

**1. Fundus Changes.**—Of 4 cases which had fundoscopic examination none of the changes described by Newman (1948) and attributed to McArdle were seen.

**2. Chest Radiography.**—The patients are mostly too ill for good-quality films to be obtained, and though physical signs can be found the results of chest films are disappointing. Two cases showed definite X-ray changes and in *Fig.* 132 the snow-storm effect can be seen in both fields. This was the chest film from *Case* 9, which died.

**3. Examination of Urine.**—Fat was found in the urine in only 2 cases.

Other examinations such as lung puncture and examination of the sputum were not carried out.

## PROGNOSIS

Out of 9 cases there were 3 deaths. All three passed rapidly into profound coma and died within twenty-four hours.

It would seem as if the patients were overwhelmed by the sudden appearance in the circulation of large quantities of fat. Cases have been described as having showers of emboli, but that has not been

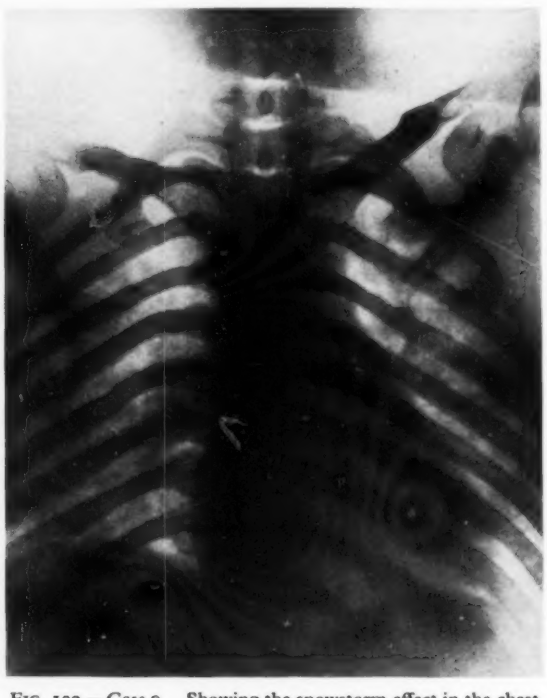

FIG. 132.— *Case* 9. Showing the snowstorm effect in the chest radiograph produced by fat embolism.

seen in any one of these cases. Cases suffer different degrees of embolism and the outcome is determined in the first hour. Cases in coma may pass into deeper coma as the fat globules cause irritation and increase in intracranial pressure, e.g., *Case* 3, where the limbs were spastic in the early stages but later became flaccid, with a C.S.F. pressure of 200 mm. of water. Cases which do not become deeply comatose, although they may have extensive brain involvement, e.g., *Case* 4 with hemiplegia, have a good prognosis. This patient still has some clumsiness of the affected hand fifteen months afterwards, but the remainder who survived have no trace of the signs in the nervous system.

## TREATMENT

Much experimental work has been done in an attempt to find a method of attacking the fat in the circulation and breaking it up into smaller particles. None of these has proved successful. It is doubtful if any substance such as a detergent powerful enough to affect the fat droplets could be introduced into the circulation without doing grave harm to other tissues.

Newman has suggested tying the profunda femoris vein in the hope of preventing further absorption of fat from the fracture. He states that it is rather like shutting the stable door after the horse has bolted. He reports 2 cases in which this was tried. The first patient survived, but perusal of the details show that the patient was delirious and not deeply comatose and would have had therefore a good prognosis. The second was deeply comatose and was overwhelmed from the start.

In the milder cases a great deal can be done to lessen the effects of the widespread embolism. In this series it was assumed that there would be no further embolism and the treatment was planned accordingly. The patient should be sedated with soluble barbitone or chloral hydrate to prevent him from further injuring the fractured limb. If irritable he should be nursed in a quiet room with a minimum of outside stimuli. A free fluid intake can usually be managed as the patient is thirsty and will respond to simple commands. If necessary an intravenous drip is set up to help elimination by the kidneys and to combat acidosis. Penicillin in adequate doses is given to control the danger of infection in the lungs.

## PATHOLOGY

This is most conveniently considered, as in previous articles, under the following headings: (1) The source of the fat; (2) The mode of entry into the circulation; (3) The cause of the entry into the circulation; (4) The effects produced.

**1. The Source of the Fat.**—Cases have been described where fat emboli have been seen in the lungs of patients suffering from a wide variety of conditions such as diabetes, burns, etc. The common clinical condition is that associated with fractures of the long bones, particularly those of the lower limbs. Wilson and Salisbury (1944) report one case where the fracture was in the upper humerus, and in *Case* 8 of this series the fracture was in the ischium. No special reason can be advanced for this affinity for the lower limbs except that in young adults, who are most prone to fat embolism, lower-limb fractures are common and the tibia and femur are large bones containing an oily fat. Large quantities of fat are seen in the fracture hæmatomas of these bones. The fact that most cases are associated with fractures, and the rarity of fat embolism without a fracture, even in the presence of extensive soft-tissue damage, makes it almost certain that the bone-marrow is the source of the fat. It is true that there is no relationship between the type of fracture and the incidence of fat embolism, making it difficult to see why one case should develop it and another escape. The work of Lehmann and Moore (1927), based on their experience of injecting dogs with cotton-seed oil, suggested that there was insufficient fat in the human femur to produce symptoms even if it all entered the circulation.

Carr and Johnson (1935) describe a fatal case where 50 c.c. of cotton-seed oil was injected into the urethra. It can be assumed that all of this did not pass into the circulation and yet it was sufficient to produce a fatality. The author recently had the opportunity of observing a patient who, in the course of intravenous pyelography, was injected with an iodized oily substance in mistake for the correct solution. This substance consisted of the iodized ethyl esters of fatty acids of poppy-seed oil, with a specific gravity of 1·27. Within an hour of the

injection the patient became restless and slightly cyanosed and the temperature rose to 101°. The appearance was strikingly similar to that of a patient in the early stages of fat embolism. It would seem that this patient had a mild oil embolism produced by 15 c.c. of a thin oil.

These two cases suggest that the human is less tolerant of intravenous oils than the dog.

**2. The Mode of Entry.**—The mode of entry of the fat into the blood-stream has also been the subject of much experiment. Tocantins (1943) has shown that the marrow cavity communicates directly with the venous circulation. Dyes injected into the marrow appear in the circulation almost as quickly as if given intravenously. Blood transfusions can be given satisfactorily into the bone-marrow and there seems no reason why the oily fat released from the bone-marrow following a fracture should not pass into the circulation.

**3. The Cause of the Entry.**—The local factors which cause the fat to enter the blood-stream have given rise to much speculation. Tension in a fracture hæmatoma is common experience, and this may be sufficient to make the contained blood and fat spurt out when the hæmatoma is entered. Such a case was *Case* 9, where at post-mortem a fracture hæmatoma under tension and containing fat was found. Fat embolism is seen in cases of compound fracture where no tension has occurred because of the wound. It may be that, although a fracture has been compound, when the wound is closed and the limb bandaged or encased in plaster, sufficient tension is created to force the fat into the blood-stream.

In short, once a fracture has been produced all the factors needed to produce embolism are readily at hand and the wonder is that it does not occur more often than it does.

**4. The Effects Produced.**—Having reached the venous circulation the fat travels to the right side of the heart and to the lungs. This produces the characteristic symptoms of restlessness and cyanosis with, frequently, dyspnœa. These symptoms are seen in any form of pulmonary embolism. Within a short time the fat may pass into the air sacs and thence to the sputum. Sections of the lung in fat embolism show large quantities of fat in the capillaries, and although it has been suggested that the fat reaches the left side of the heart via a patent foramen ovale there seems no reason why it should not pass through the pulmonary capillaries. This would agree with the clinical findings where the patient first develops symptoms of a chest disorder followed by the signs of widespread arterial embolism. Having reached the arterial system, the fat is distributed to those parts of the body with the best blood-supply, including the brain, kidneys, and heart. In these organs are most frequently found the petechial hæmorrhages which stain for fat.

The distribution to the skin of the root of the neck and chest allows of no logical explanation. With the patient prone, the thyroid axis artery, which gives rise to most of the branches supplying skin in this region, passes directly forwards from the subclavian, and it may be that the physical properties of the fat allow it to pass more easily into this vessel.

In the brain the petechial hæmorrhages are seen in the white matter where the vessels are end-arteries. The fat must also disturb the function of the grey matter though petechiæ are not seen there.

The changes which occur in the fat once it has become lodged have been very adequately described by Wilson and Salisbury (1944). These consist of breaking up of the fat into its component fatty acids with local irritation and cellular response.

## CASE REPORTS

*Case* 1.—A 43-year-old man was admitted with compound fractures of both lower legs caused by a road accident. Because of his poor general condition the wounds were dressed and the limbs splinted and toilet, with reduction and plaster fixation, carried out the following day. Seventy-two hours after the injury he became restless and complained of dyspnœa. He was found to have a temperature of 100·6° and cyanosis of the lips. A petechial rash of a small type appeared over the upper part of the chest and both shoulders. He was not known to have been incontinent. Moist sounds were heard in the lungs, but no X-ray changes were seen. He gradually improved, and five days later was well enough to have a skin slough excised and grafted. There is now no evidence of the fat embolism.

*Case* 2.—A 22-year-old man was involved in a motor-cycle accident and was admitted to hospital with several soft-tissue wounds and fractures of one femur and the opposite ulna. The wounds were excised and the fractures manipulated. The femur was immobilized in a Thomas splint with skeletal traction and the forearm fixed in plaster. On the third day the temperature rose suddenly and the patient was drowsy. He was not known to have been incontinent and a search for the cause of the temperature revealed a petechial rash over the shoulders. This faded within the following week, the temperature settled, and his subsequent treatment was uneventful. There are now no residual findings in the central nervous system.

*Case* 3.—A 19-year-old man was admitted following a motor-cycle accident in which he was the pillion rider and *Case* 4 the driver. He was found to have a compound fracture of the right femur and a fracture of the right tibia. He was treated for shock and two hours later the wound was excised and the fractures were immobilized in a Thomas splint with skeletal traction and a below-knee plaster. Twenty-four hours later he suddenly passed into a deep coma and when seen an hour later was deeply unconscious with a temperature of 101°. The pupils were small and there was rotatory nystagmus. The limbs were spastic and despite the raised temperature the skin was strikingly pale, suggesting a disturbance of the temperature-regulating mechanism. The patient was incontinent. Moist sounds were present in the chest. There were no changes in the fundi. The following day despite intravenous infusion the coma deepened, the temperature rose to 102°, and petechiæ were found in the conjunctival sac of both lower lids. Lumbar puncture showed a pressure of 200 mm. of water. During the subsequent twelve hours the coma deepened, the temperature and pulse rose further, and the limbs became flaccid and the pupils dilated, suggesting increased intracranial pressure. Post-mortem revealed widespread fat embolism with petechiæ in the white matter of the brain and lungs. One pleural cavity contained blood, on the surface of which fat could be seen floating in considerable quantities. Both fractures were surrounded by a hæmatoma in which fat could be seen with the naked eye. The petechial hæmorrhages all stained heavily for fat.

*Case* 4.—A 23-year-old man was admitted from the same accident as involved *Case* 3. He had been the driver

of the motor-cycle. He was found to have a fracture-dislocation of the right hip and a fracture of the upper end of the right tibia with a disorganized knee-joint. After shock treatment the dislocated hip was reduced and the fracture of the tibia manipulated. A hip spica was applied and the patient returned to the ward. Twenty-four hours later a displaced fracture of the neck of the fifth right metacarpal was manipulated under light gas and oxygen and a plaster applied. Forty-eight hours later the patient became restless and apprehensive and the temperature rose to 101°. Examination of the skin showed petechial hæmorrhages in the posterior triangle of the neck on one side. There was a left-sided hemiplegia and deviation of the tongue, but no changes in the pupils, fundi, or conjunctivæ. The temperature continued to swing during the subsequent week and although the hemiplegia had improved within three days the patient remained incontinent for a further ten days. At the end of six weeks the hemiplegia had passed off, except for slight weakness of the face and inability to distinguish temperature in the hand. This abnormal sensation in the hand was still present fifteen months later.

*Case* 5.—A 28-year-old airman was admitted following a motor-cycle accident. He was found to have a fracture of the upper third of the left femur. This was treated by manipulation and fixation in a Thomas splint with skeletal traction. Thirty-six hours later he lapsed into unconsciousness and became incontinent. He could be roused with some difficulty but was irrational and when left alone became stuporose. There was cyanosis of the lips and patchy consolidation of both lungs. There was a petechial rash over the upper chest and in the triangles of the neck. There was slight weakness of the right side of the face, the pupils were unequal, the fundi normal, and the left plantar response was extensor. The chest radiograph showed patchy consolidation. The patient was nursed in a quiet room and though irrational and difficult could be made to drink freely. He was kept heavily sedated and he gradually became manageable. The temperature swung between normal and 100·8°, but settled on the fifth day when he became conscious. The plantar response was found to be flexor twelve hours after the first examination. The inequality of the pupils remained and subsequent inquiry from the patient revealed that this had been present for many years. His progress was uneventful and there are no residual signs.

*Case* 6.—A 45-year-old man was admitted after being knocked down by a motor-cycle. He was found to have a compound fracture of the right tibia. The wound was excised and sutured and the limb immobilized in plaster. The patient was well the same evening and had a good night. The following afternoon, 24 hours after the reduction, he developed a temperature of 101° and was noisy and irrational during the night. The following morning he was found to be drowsy and incontinent and there was a widespread rash over the chest and shoulders. The patient would answer questions but was confused. No physical signs were found in the central nervous system, and the fundi were normal. Moist sounds were heard in the chest, but a radiograph showed clear lung fields. The patient was sedated the next evening and had a quiet night. The drowsiness passed off the following day and he became continent. The temperature settled on the third day. His progress has since been uneventful and there are no sequelæ. The temperature chart and the rash in this case are recorded in *Figs.* 130, 131.

*Case* 7.—A 4-year-old boy was admitted with a fracture of the shaft of the left femur sustained when he fell over a playmate. The limb was immobilized in a Thomas splint with skin traction. Thirty-six hours later he was found to be drowsy and incontinent. There was no rise in temperature but the pulse-rate rose from 92 to 148 per min. No skin rash was found and there were no signs in the central nervous system. A specimen of urine contained fat. The child remained drowsy for two days and then became continent and seemed to be himself again. For the following month he had short attacks of unconsciousness lasting from a few seconds to ten minutes. There had been no previous history of attacks and they gradually became less frequent and disappeared in a month. The condition was most suggestive of petit mal precipitated by fat embolism.

*Case* 8.—A boy aged 6 was admitted after having been crushed by a small steam roller. There were extensive soft-tissue wounds of the legs and a laceration in the perineum with a fracture of the inferior ramus of the ischium. The wounds were excised and sutured and a catheter passed to exclude damage to the bladder and urethra. The child came round from the anæsthetic and went to sleep normally. Six hours later he was found unconscious with cyanosis and moist sounds in the chest. The temperature and pulse were elevated and during the next four hours rose as the coma deepened. He died shortly afterwards and at post-mortem extensive fat embolism of the lungs and kidneys were found. The white matter of the brain showed areas of congestion which did not stain for fat.

*Case* 9.—A girl of 19 was admitted with lacerations of her scalp and face and a fracture of the shaft of the left tibia, sustained when her bicycle collided with a wall. The lacerations were sutured and the fracture reduced and plastered. The following day her temperature rose suddenly to 101·2° and she became drowsy. Moist sounds were found all over the chest and a radiograph revealed the snowstorm effect seen in *Fig.* 132. A petechial rash appeared over the chest and shoulders and the patient became steadily more comatose and incontinent. Fat globules were found in the urine. The patient died the following day and at post-mortem widespread petechial hæmorrhages were found in the brain, the lungs, and the kidneys. Examination of the fracture showed that the periosteum was intact and when the fracture hæmatoma was opened the contents spurted out, showing that there had been considerable tension; fat could be seen in the blood.

## SUMMARY

1. The incidence of fat embolism is discussed.
2. The characteristic symptoms of sudden change in mental state, dyspnœa, a rise in temperature, and the development of incontinence are described.
3. The physical signs are seen in the skin and conjunctiva, the chest, and in the central nervous system.
4. The skin rash is described.
5. The pathology of fat embolism is discussed with reference to the clinical findings.
6. Nine cases are reported.

My thanks are due to all members of the staff of the Robert Jones and Agnes Hunt Orthopædic Hospital for their permission to see and publish details of their cases. Mr. G. K. Rose and Mr. F. Brian Thomas have kindly supplied me with details of cases treated by them in their own traumatic units.

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# ACUTE OSTEOMYELITIS IN INFANCY AND EARLY CHILDHOOD

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IT has been estimated that 90 per cent of cases of acute osteomyelitis occur during childhood and adolescence, and that the great majority of these cases appear between the ages of 8 years and 16 years (Montgomery, 1948). Pyrah and Pain (1933), reviewing 262 cases, found the majority in a slightly younger age group, 5 to 14 years, but Fraser (1924) placed the majority of his cases in the more contracted age group of 8 to 12 years. This age susceptibility has been attributed to the anatomic structure of growing bone coupled with a poor resistance to infection. The occurrence of acute osteomyelitis in infancy and early childhood is not uncommon, but it is only within recent years that acute osteomyelitis in infancy (including the newborn period) has attracted special mention, with the exception of acute osteomyelitis of the maxilla which for a long time continued to be studied; in the newborn this was practically the only kind reported (Bass, 1928; Poucher and Blayney, 1934). Green (1935), however, remarked that acute osteomyelitis in infancy differs so much from the disease in older children that in infants under 2 years of age " separate consideration of the disease . . . is desirable ".

During the past twenty-two years (1930 to 1951 inclusive) 40 cases of osteomyelitis were admitted to the Duchess of York Hospital for Babies which takes in-patients limited to the 0–5 years age group. The age distribution of these 40 cases is shown in *Fig.* 133, from which it can be seen that the greatest number fall into the age group 0–6 months. Relatively few cases occurred after the thirtieth month of life. Four of the cases in the 0–6 months group were neonates.

## AETIOLOGY

In childhood the inflammation in the bone is, in the vast majority of cases, initiated by staphylococci, *aureus* usually, *citreus* or *albus* rarely; streptococci and pneumococci are responsible in a small percentage, and occasionally the typhoid or colon bacillus has been guilty, and mixed infections do occur (Montgomery, 1948). Camera (quoted by Santi, 1934) had a case due to *B. coli*, and Leichentritt (quoted by Santi) one due to *B. fæcalis alkalinus.*

Donovan (1940) states that staphylococci and streptococci account for 90 per cent of cases and that staphylococci are commoner in older children and streptococci in infants, and adds that *H. influenzæ* has been a cause. Fraser (1924) reported the following incidence of pathogenic organisms in 400 cases: *S. aureus*, 78 per cent; *S. albus*, 2 per cent; *S. pyogenes*, 6 per cent; Pneumococcus, 14 per cent; *B. coli communis*, 1 case; *B. typhosus*, 3 cases. The percentage for the pneumococcus was rather striking, but Fraser did not attempt to show a predominance of any particular organism for any particular age group.

In the series of cases under review, a mixed infection by hæmolytic streptococcus and staphylococcus was present in 4 cases; *S. aureus* in pure growth was cultured from 5 cases, which included 1 neonate. A streptococcus was the agent in 3 other cases, and a pneumococcus in pure growth was found in another neonate, prematurely born.

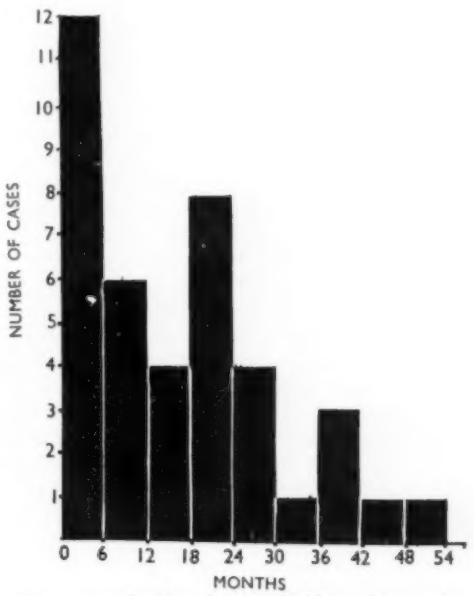



FIG. 133.—Showing the age incidence in months of 40 cases of osteomyelitis occurring during a period of twenty years.

Blood-cultures were not usually done in this series, and the one positive culture grew a *S. aureus*; this was from a case in the 0–6 months age group.

Osteomyelitis in the newly born has been frequently secondary to umbilical infection. Fraser stressed the importance of umbilical sepsis in 1924 when, judging from his comments, this importance was not well recognized. He had collected 30 cases of osteomyelitis in infants in whom umbilical sepsis complicated by pyæmia was the underlying cause of the bone pathology. These 30 cases had been collected during four years. At this time, also, there

appeared to be a disregard by midwives towards the umbilical cord stump and this probably accounted for the majority of cases among infants. Palew (1931) attributed the only case, as far as I am aware, of gonococcal osteomyelitis to this portal of entry, and was inclined to attach the blame to a midwife who was probably a carrier of the gonococcus.

The not uncommon occurrence of osteomyelitis of the maxilla has been ascribed in large part to pathogens derived from the infected maternal breast (Marx, 1920). This may be a valid postulate in many cases, but in one case of osteomyelitis of the maxilla of this series the child was 2½ years of age and had for long lost contact with this source.

Boils, infected blisters, and abrasions of the skin can be factors, but such foci of infection may have healed by the time the osseous lesion shows. In the 40 cases here reported on, 2 began with abscesses of the neck, 1 with a bilateral purulent otitis media, 1 with a paronychia, 1 with an impetiginous skin rash, 1 with umbilical sepsis, 1 with an abscess of the thigh, 1 with a septic finger, and 1 with a septic toe, but in many cases no focus for the initial infection was detected although there was evidence of a healed sore on the hand of one case, and a few papules on the forearm of another, who also had a scab on the lower lip.

Greengard (1946) wrote on 10 cases, aged 2 weeks, 7 weeks, 3 months, 4 months, 7 months, 9 months, 11 months, 11 months, 18 months, and 22 months, in whom the sites of initial infection were otitis media with parotitis, none, none, infective diarrhœa, pneumonia with empyema, pneumonia, pneumonia and empyema, cervical adenitis, upper respiratory tract infection, and injury to leg, respectively.

Montgomery and also Donovan regard osteomyelitis as more common in children from the poorer strata of society—strata in which little, if any, attention to hygiene of the skin is paid; but Chapple (1946) does not attach any importance to the economic state of the patient. Perhaps it is not without relevance to remark that of the 40 cases receiving mention here the large majority came from rather poor homes with few ablution facilities; in contrast to this, however, is the fact that three of the neonates were direct transfers from newborn nurseries. It is worth mentioning here Santi's reference to published reports of intra-uterine infection producing congenital osteomyelitis.

Pyrah and Pain (1933), in their review of 262 cases, found trauma to be a predisposing factor in a high proportion of cases, but Wakeley (1932) was of the opinion that trauma played little or no part. In only 3 of my 40 cases could the possibility of trauma be recalled; in 2 older children a fall had preceded the osteomyelitis and in the third case the patient had sustained a direct blow to his foot. These 3 cases apart, trauma of any kind appears to have played a negligible part and suggests that in the 0 to 5 years age group it is only very occasionally of significance.

Fraser estimated the sex incidence of his cases to be in the ratio of one female to six males. Chapple (1946) has it that males are involved twice as often as females, but that there is no such sex linkage in infancy. This latter statement is substantiated by the sex ratio of my 40 cases, which were comprised of 22 males and 18 females. Such observations lend support to the opinion that the preponderance of males in the older age groups is due to their greater liability to trauma, although Wakeley denies trauma to be of significance, as has already been mentioned, and had come to the conclusion that osteomyelitis was "a disappearing disease".

## PATHOLOGY

The metaphysis is most often affected because of the rich blood-supply. The blood-vessels are especially numerous in this part of the long bone in infancy but they do not extend into the epiphysis; these vessels are end-vessels, they do not, in very early life, communicate with the vessels supplying the spongiosa. This vascular arrangement slows the stream of blood and permits the deposit of groups of organisms like the staphylococcus or streptococcus, and the low resistance of the metaphysis favours the development of osteomyelitis. In infancy the epiphysial cartilage is relatively thick and is a very effective barrier to joint involvement. The older the child the thinner this barrier of cartilage becomes, and this fact renders the older child, or adolescent, in whom the epiphyses are about to fuse with the shaft, more likely to develop a secondary arthritis. This is the reason for secondary arthritis being so uncommon in early childhood and infancy, in which time of life it occurs only if the joint capsule includes some part of the metaphysis, like the hip-joint, for example.

*Table I.*—INCIDENCE OF BONES INVOLVED

| *Bones involved* | *Number of cases* |
|---|---|
| Maxilla | 3 |
| Maxilla and zygoma | 1 |
| Sternum | 1 |
| Ribs | 1 |
| Humerus | 2 |
| Radius | 1 |
| Radius and ulna | 1 |
| Radius and ulna and metatarsa | 1 |
| Femur | 11 |
| Both femora | 1 |
| Femur and sternum | 1 |
| Femur and ilium | 1 |
| Femur and os calcaneus | 2 |
| Femur and ribs | 1 |
| Femur and tibia and fibula | 1 |
| Tibia | 3 |
| Fibula | 2 |
| Tibia and fibula | 1 |
| Metatarsal | 1 |
| Phalanx: | |
| Terminal, great toe | 1 |
| Finger | 1 |
| Humeri, radius, ulna, femora, tibiæ, and metatarsal | 1 |
| Femora, hip-joints, radius, sternum, ribs, sternoclavicular joint | 1 |
| Total | 40 |
| Deaths (at ages 10 days, 1 month, 6 weeks, 2 months) | 4 |
| Mortality: | |
| Overall | 10 per cent |
| Under 6 months of age | 36 per cent |

The upper end of tibia, lower end of femur, lower ends of tibia and fibula, upper end of humerus, lower end of radius, lower end of humerus, upper end of femur, and less often of ulna, the pelvic bones, and ribs are affected in that order. But Santi's 366 cases of 10 years of age and under gave precedence to the upper end of femur, followed by

humerus, tibia, radius, ulna, in order; other bones were much less often affected.

Osteomyelitis of the vertebra has been described by Madier (1922), and Baumgartner (1920) and Broca (quoted by Baumgartner) have reported primary acute osteomyelitis of the skull. The bones of the hands and feet have rarely been affected (Cass, 1940). In the severe cases the infection may successfully attack one or more additional bones at varying intervals of time.

*Table I* shows the incidence of the bones involved in the 40 cases under analysis. The femur was attacked 11 times and both femora on 1 occasion, a striking preponderance of this over other bones, and this preponderance is greater still if the cases with multiple foci, which include the femur, be added (*Table II*).

*Table II.*—The Relative Frequency of Involvement of Skeletal Components

| | *Cases* |
|---|---|
| Femur | 20 |
| Radius | 5 |
| Tibia | 4 |
| Maxilla | 4 |
| Sternum | 3 |
| Ribs | 3 |
| Ulna | 3 |
| Metatarsal | 3 |
| Fibula | 3 |
| Humerus | 2 |
| Os calcaneus | 2 |
| Phalanx | 2 |
| Ilium | 1 |
| Hip-joint | 1 |
| Sternoclavicular joint | 1 |
| Zygoma | 1 |

Osteomyelitis in infants differs importantly from osteomyelitis in older children. The thin, less compact corticalis of infants allows earlier spread to the subperiosteal space, and the more delicate loosely attached periosteum permits earlier subperiosteal abscess formation and rupture (or ' decompression ') into the soft tissues (Caffey, 1945). These factors also encourage spontaneous drainage of the bone shaft, and this fact prevents necrosis and sequestrum formation which is a characteristically absent feature from acute osteomyelitis of the long bones in infancy.

Fraser (1924) alluded to the probability of sepsis in the newborn being the cause of osteomyelitis in later life, and Dillehunt (1935) was convinced that acute osteomyelitis is "a disease exclusive of children" and that in adults it is probably due to a lighting up of an infection acquired in childhood.

## PROGNOSIS

Usually the localized mild acute osteomyelitis without sequestrum formation may heal completely, if properly treated, in 7 to 10 weeks, the more diffuse form may continue for several months (Montgomery). Green (1935) gave an average of 3 months for complete healing after operation, but frequently the healing took only 4 to 6 weeks. It is not possible to be sure, however, that an apparently well-healed bone will not relapse months or even years later (Montgomery, 1948; Fraser, 1924; Dillehunt, 1935).

In infants the disease may show relatively little clinical disturbance even when the roentgen picture depicts gross osseous change, and the prognosis with or without active treatment is good (Dillehunt; Cass, 1940) or excellent according to Caffey (1945), although arthritis, fracture, dislocation, and growth disturbances, either elongation or shortening of the affected bone, may follow. Green also regards the prognosis as excellent if the child survives the systemic upheaval, so common in his series.

Dillehunt also regarded the disease in infants as relatively benign, and failure to treat it in infants as not having the serious consequences which afflict adults. Cass (1940) reported 3 cases of newly born infants who suffered little, if any, systemic distress even when multiple foci were present, and Stone's (1942) 4 cases recovered. Stone believed treatment of the bone lesion to be of secondary importance and that in the newborn the disease is benign, but Green's figures are interesting in this respect. He gives a mortality of 21 per cent of 95 cases occurring in infancy (0–2 years of age) but the mortality was 44 per cent for babies under 6 months of age and 13·4 per cent for infants between 6 months and 2 years of age. However, he was able to reduce this mortality to 6·6 per cent in a series of 32 infant cases which were treated in a period of four years. He stresses the primary importance of supportive measures and treatment to combat the general illness. Paschlau (1932) had a series of cases in infants of which 38 per cent died, and 53 per cent of Santi's (1934) series under 1 year of age succumbed.

Greengard (1946), when he published details of 10 cases, divided osteomyelitis in young children and infants into two groups: the benign group with little or no complaint other than the local lesion; and a group with evidence of severe systemic disturbance of which the local bone lesion is a complication. Hutter (1948) was of like opinion when he reported 3 neonates with acute osteomyelitis. Dunham (1933) had 4 cases of septicæmia who developed acute osteomyelitis; 3 of these died. Mount (1935) had 1 case of septicæmia complicated by secondary osteomyelitis of the humerus, also fatal. Fraser, too, thought that acute osteomyelitis in the very young differed from older cases in that the local condition was a complication of septicæmia derived from umbilical sepsis. Yet Thomson and Lewis (1950) were able to present 4 cases of prematurely born neonates, only 1 case of which died.

Four of the 40 cases admitted to this hospital died, a mortality of 10 per cent, and the ages of these infants were ten days, one month, six weeks, and two months, or of the small number of neonates 50 per cent, of the 0–3 months age group 44·4 per cent, and of the 0–6 months age group 36·3 per cent, figures which show a progressive falling off of the mortality, which was nil after 3 months of age.

## DISCUSSION

Hart (1937), in his general discourse on acute hæmatogenous osteomyelitis in children, presents the anatomic, clinico-pathological, and pathogenetic features of the disease in children, but, other than a brief reference to Green's paper, makes no special application to infants or very young children.

What is clear from the published cases of osteomyelitis in infants is that the disease has features peculiar to this early age, but that these features are not constant from case to case and that one can be too dogmatic.

Dillehunt called attention to the fact that acute osteomyelitis is rarely diagnosed sufficiently early to prevent gross destruction and the attendant complications. He emphasized the rareness of the condition in infants, but postulated an alternative—that the dearth of reported cases was due to its greater incidence remaining unrecognized. This was as recently as 1935. His experience with 300 cases of subacute or chronic cases had shown that in almost every instance the acute phase had not been detected and for this reason he laid down a dictum: "If a child under 13 years of age is seized with pain in an extremity and he shows loss of function, elevation of temperature, and leucocytosis, that child has acute osteomyelitis". His survey of the literature for the eighteen years preceding 1935 had disclosed very few reports of acute osteomyelitis of the long bones in young children, and only 1 case, which was an infant, yet he was able to give 3 cases in infants under 6 months of age from his own experience, 2 of these were less than 6 weeks old.

Wade, writing in 1929, does not present one case in an infant, yet he stated that the incidence in infants is in the 0–3 months age group and that after this age no cases are seen until the age of 2 years. Such a statement is invalid, but nevertheless could at that time be made with apparent justification.

That sequestrum formation does not take place, or if it does is quickly resolved, is a fair observation, but in this connexion Baumgartner's experience with osteomyelitis of the skull is worth mentioning. His infant extruded on two occasions rather large pieces of necrosed skull bone. Only 6 of Green's 95 cases developed gross sequestra.

*Table III* shows the annual incidence of the 40 cases admitted to the Duchess of York Hospital from 1930 to 1951 inclusive, an average of 1·8 cases per year. All the cases were under 5 years of age.

*Table III.*—Showing Annual Incidence, 1930–1951 Inclusive

| *Year* | *Number of cases* |
|---|---|
| 1930 | 3 |
| 1931 | 3 |
| 1933 | 1 |
| 1935 | 1 |
| 1936 | 3 |
| 1937 | 1 |
| 1940 | 1 |
| 1941 | 2 |
| 1942 | 2 |
| 1944 | 1 |
| 1945 | 3 |
| 1946 | 2 |
| 1947 | 3 |
| 1948 | 5 |
| 1949 | 2 |
| 1950 | 4 |
| 1951 | 3 |
| Total | 40 |

There were five years, 1932, 1934, 1938, 1939, and 1943, in which no cases were admitted. This table shows that in infancy and early childhood acute osteomyelitis is not very uncommon and that in the neonate it is rare, which supports Dillehunt's observation in 1935, which seems just as valid to-day.

The impression has been established firmly enough to make its incorporation into text-books (Chapple, Donovan, Montgomery), that in infancy the streptococcus predominates as the responsible micro-organism. Green, in 95 infants, found the streptococcus in 63 per cent. Greengard (1946), in 6 cases with positive blood-cultures, did not have a single case infected by the streptococcus, but all by staphylococci. In the 4 premature babies described by Thomson and Lewis (1950) the organism was isolated in 3 and shown to be staphylococci. Shulman's (1946) neonate was infected by *S. aureus*, and 2 of Dillehunt's 3 cases aged 6 months and 4 weeks had *S. aureus*, the third aged 5 weeks gave a growth of streptococcus.

The hæmolytic staphylococcus was isolated on blood-culture from Mount's case aged 12 days, and Baumgartner's case aged 4 months grew a staphylococcus.

The 3 newly-born cases reported by Cass (1940) were infected by *S. aureus*. In the relatively few of the 40 cases in which blood-culture was carried out or from which pus was removed for examination, a streptococcus alone was not isolated; all, except one, a pneumococcus in pure culture from a premature baby, were either *staphylococcus aureus*, or pyogenes or, on occasions, a mixed infection of staphylococci and streptococci.

A reasonable deduction to make from these data is as follows: In the newborn and young infant the very common pathogenic organism which gives rise to a septicæmia and a localization of infection in bone is the staphylococcus, which when it is not pathogenic is practically a skin commensual. It is the older infant and younger child who is liable to develop an osteomyelitis as a sequel to a blood-borne infection derived from streptococci, so commonly found in the upper respiratory tract and air spaces. It is probably about the 2-year age limit that this transition takes place. Fifty-five per cent of Green's 95 cases gave definite evidence of antecedent infection, half of which were respiratory disorders.

In the older child and adolescent acute osteomyelitis is accompanied by fever, leucocytosis, and local tenderness. This triad is not, however, an invariable accompaniment of the disease in the very young age group. Only 13 of the 40 cases had a temperature raised to febrile level on admission to hospital, although subfebrile temperatures were almost the rule, that is, temperatures hovering about 99° to 100° F. In 23 instances only was the white blood-cell count done and neither the total nor the differential counts exhibited any constant relationship with the mildness or severity of the general or local condition. The white blood-cell count ranged from 5000 to 40,000 in different cases and the polymorphonuclear leucocytes from as few as 30 per cent to as many as 80 per cent. Local tenderness over the bone lesion was in some cases readily detectable, in others careful examination was necessary, for in infants in the early stage the only localizing symptom is tenderness; signs such as erythema, swelling, and even loss of function appear relatively late.

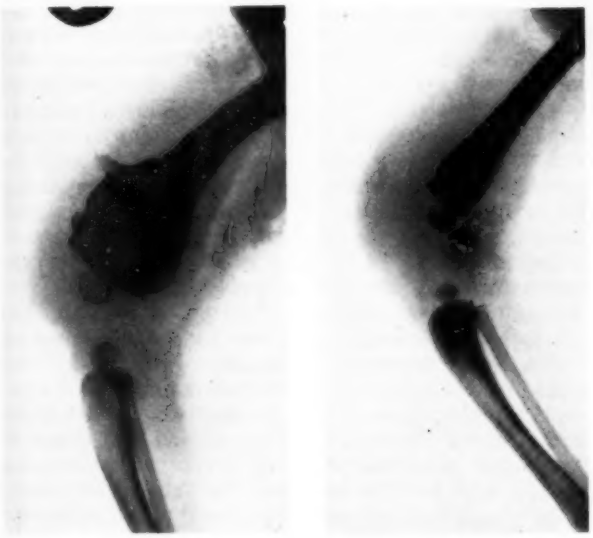
On the few occasions when the erythrocyte sedimentation rate was estimated, it was raised, except in 1 case.

In many cases the onset was insidious, the infant or child going off its food, showing a disinclination to walk if it had previously done so, perhaps a general malaise with or without slight feverishness and loss of weight. This symptomatology, so

common for many different complaints in young children, not uncommonly preceded signs of the local lesion by a week or more. Only occasionally did the osteomyelitis manifest in a fulminant manner, with high fever, vomiting, and convulsions.

On the whole there were very few complications of the bone lesion itself; one pathological fracture and one bilateral suppurative arthritis of the hip-joint resulting in destruction of the femoral heads.

It remains doubtful whether the advent of the numerous antibiotics has served to make any noticeable difference in the results of treatment of acute



A B

FIG. 134.—Showing: A, Roentgen evidence of early osteomyelitis of distal metaphysis of femur; and B, The roentgen appearance a few weeks later after a course of penicillin treatment without any surgical intervention.

osteomyelitis in infancy and very young children. Where the osteomyelitis is a complication of a systemic blood-borne infection appropriate antibiotic or sulphur-drug therapy might prove life-saving and so help to reduce the mortality; but where the benign local lesion is the primary objective of therapy simple surgical intervention is still the procedure of choice when practicable. Reluctance to interfere surgically because the infecting micro-organism has been shown to be sensitive to one or other antibiotic does not, *ipso facto*, improve the therapeutic result, but on the contrary may lead to a profuse overgrowth of osseous tissue (involucrum) about the focus of infection in a long bone (*see Fig.* 134), whereas evacuation of pus by use of the scalpel or syringe usually gives a gratifying rapid healing, but there is no objection, indeed it may be considered advisable, to cover surgical treatment with an antibiotic in order to arrest or prevent any possible subclinical pyogenic metastasis.

We cannot ignore a fact, however, to which Green drew attention in 1935, that "early drainage of the bone does not decrease the amount of destruction nor does it limit the systemic manifestations. On the other hand, poorly timed extensive surgery jeopardizes the child's life. There is no haste in performing an operation and operative procedures must be minimal".

Definitive localization of the bone lesion, because of the anatomic structure, as already outlined, occurs quickly, and it is unnecessary to do more than adequately drain the secondary abscess in the soft tissues.

## SUMMARY

An account is given of acute osteomyelitis as it occurs in infancy and early childhood, in which age the clinical picture differs remarkably from the disease as it occurs in older children. Cases which have appeared in the literature are briefly reviewed, and the rather recent recognition of the disease as it occurs in the long bones pointed out.

Special reference is made to a series of 40 cases under 5 years of age in drawing comparisons with clinical and other features which heretofore have been remarked upon in the literature. A general discussion of such features follows.

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## *EXPERIMENTAL SURGERY*

# AN ATTEMPT TO PRODUCE PEPTIC ULCER BY PHRENIC–VAGUS ANASTOMOSIS IN DOGS

By T. STEWART HESLOP, B. SCHOFIELD, W. THORPE CATTON, D. E. WRIGHT, and PAMELA A. BURSTALL*

One of the greatest obstacles in the experimental study of peptic ulcer has been the production of a form of ulceration which bears some resemblance to the disease in man. In animals, chronic gastric ulcers can be produced by three main techniques :—

1. By increasing the output of parietal secretion and therefore the acidity of the gastric contents over long periods of time. The most successful techniques of this type are those in which histamine is injected in beeswax mixture to prolong the action of the drug.

2. By allowing the unneutralized gastric juice to play on a portion of the gastro-intestinal tract not accustomed to receive it. The Mann-Williamson dog is the best known preparation of this type.

3. By the use of the drug cinchophen, the mode of action of which must still be regarded as uncertain.

None of these methods presents a really satisfactory parallel with known features of the aetiology of peptic ulcer, but the Mann-Williamson dog has become the standard technique for the assessment of anti-ulcer therapy in the laboratory.

Ever since the clinical correlation between gastric hæmorrhage and lesions in the brain was first noted in the early years of the last century, the view has existed that peptic ulceration may be partly or wholly due to nervous factors. It is not certain who first put forward this idea, but Ivy, Grossman, and Bachrach (1950) attribute it to Jäger in 1811. Since then it has been a matter of interest to both experimental workers and clinical observers, though most of its support has come from the latter. The concept was first given anatomical and physiological precision by Harvey Cushing (1932), who associated it firmly with parasympathetic centres in the diencephalon and with the vagal pathway. Recent work in man by Wolf and Wolff (1943) has thrown into great prominence the influence of psychic factors on the secretion and motility of the stomach, and clinicians have long recognized their importance in the ulcer diathesis. The recent vogue for the operation of vagotomy is based on the view that the vagus nerve is the pathway by which these influences are brought to bear on the stomach.

It is therefore surprising to find that no investigators have so far demonstrated satisfactorily that chronic peptic ulceration can be produced by long-term stimulation of the vagus nerves. Attempts have often been made and a variety of methods used. Thus Silbermann (1927) and later Schmidt and Fogelson (1937) used repeated sham feeding in œsophagotomized dogs. The vagus nerve has been stimulated electrically by Stahnke (1924), who used an intra-œsophageal electrode, and by Ettinger, Hall, and Banting (1936), and Manning, Hall, and Banting (1937), who used permanent implanted electrodes in the neck. In all cases the stimulation has been intermittent, or if continuous has been maintained only for relatively short periods. That continuity does appear to be a factor of great importance is illustrated by a comparison of the efficacy of the histamine beeswax method in producing gastric ulceration with the great difficulty with which the condition can be produced by repeated injections of histamine alone. Electrical excitation of the vagus nerves involves the difficulty of associated afferent stimulation, and long-term experiments with implanted electrodes are open to the risk of the nerve becoming ultimately damaged or sealed off by fibrosis from the stimulating current.

As a substitute for continuous vagal stimulation a number of investigators have tried the effect of prolonged administration of parasympathetic-mimetic drugs, but this approach also has not led to any reliable method of ulcer production. Pilocarpine was used by a number of early investigators. Hall, Ettinger, and Banting (1936), used acetylcholine, Wener, Hoff, and Simon (1948) mecholyl, and Hale and Grossman (1950) 'Urecholin' (urethane of β-methyl choline hydrochloride). Disadvantages of these methods are that the drugs have numerous side-effects and that, following large doses or the accumulated effect of a number of small ones, a reversal of effect may occur with inhibition of secretion (Gray and Ivy, 1937). The lesions produced by large doses of these materials seem to be primarily of vascular origin.

In the present work an attempt has been made to obtain continuous stimulation by directing the repetitive discharge from the respiratory centre on to the vagal endings in the stomach by means of a phrenic-vagus anastomosis in the chest. The advantages of such a procedure from the point of view of continuity are obvious, and it further avoids any difficulties of associated afferent stimulation. There is no reason to believe that the phrenic would not continue indefinitely to carry respiratory impulses even though detached from the diaphragm. Although it has been claimed by some workers that central nervous reintegration occurs after cross-anastomosis of nerves, the bulk of opinion is against this (Sperry, 1945).

The method depends on the establishment of a functional connexion between somatic and autonomic nerves. The early literature on nerve anastomosis contains numerous reports of successful connexions of this type. The best known are those of Langley and Anderson (1904), Erlanger (1905), and Ballance

* The present work was commenced in 1948 at the Buckston Browne Research Farm, by T. Stewart Heslop and B. Schofield, and was completed at the Department of Physiology, King's College, Newcastle upon Tyne.

(1931). Some later workers in the field have doubted these early results, following the demonstration by Evans of the very abnormal type of endings developed in the adrenal gland after hetero-innervation by a spinal nerve (Evans, 1947), but Evans himself (1949) has obtained convincing evidence of function in hypoglossal-cervical sympathetic anastomoses in the rabbit after 200 days.

The technique of phrenic anastomosis to obtain continuous stimulation was first used by Cannon, Binger, and Fitz (1914), who anastomosed the central end of the phrenic to the peripheral portion of the cervical sympathetic and produced in this way a state in cats resembling hyperthyroidism. The exact method of causation was uncertain, and a further investigation of the problem was carried out by Friedgood and Cannon (1940). They made anastomoses in 28 cats, of which 9 developed functional anastomoses, as judged by retraction of the nictitating membrane and dilatation of the pupil. Only 2 animals showed the condition described by Cannon, Binger, and Fitz, but one of these is particularly interesting since it showed an alternation of pupil size in rhythm with the respiration.

The technique was also used by Robertson and Derbyshire (1935) in an attempt to stimulate continuously the vagus and sympathetic supply to the heart in cats. They were unsuccessful in producing any anatomical or physiological change in the heart, although they kept some of their animals for over two years. Their work is interesting, since, by the use of electric recording they were able to show that phrenic impulses from the respiratory centre travelled down the anastomosed nerves as far as the level of the aortic arch.

In spite of the above it seemed desirable that the method should be given a thorough trial for the present purpose. Apart from the obvious value of the demonstration that chronic ulcer could be produced by nerve stimulation alone, the animal with a functional phrenic-vagus anastomosis might then prove a far better preparation for the assessment of anti-ulcer therapy than the Mann-Williamson dog.

Work on this problem was commenced by one of us (T. S. H.) in 1937, but after a satisfactory technique had been worked out the war intervened and the animals had to be destroyed only a few months after the anastomoses had been made. When the work was resumed in 1948 it was planned that the 4 dogs on which the present report is based should constitute a pilot experiment. Had any evidence of function in the anastomoses been obtained we had intended to set up a group of anastomoses on dogs equipped with fully innervated gastric pouches on which we could have studied in detail the anticipated increase in basal secretion and its possible relation to ulceration.

## METHODS

Mongrel dogs of weight 9–12 kg. were used. They were fed on a diet composed of boiled meat, bread, and dog biscuit. To provide evidence of the onset of function in the anastomosis, arrangements were made for the regular sampling of the basal secretion of the stomach. Three animals were provided with Mann-Bollman gastric fistulæ prepared from ileum and attached to what was estimated to be the most dependant part of the stomach when the animal occupied its normal standing position. This type of fistula was considered most suitable for the long-lasting experiment projected since it does not leak and requires no attention.

**Nerve Anastomosis.**—This was carried out approximately three months after the Mann-Bollman fistula. The animals were anæsthetized with ether–oxygen from a Tiegel-Henle positive-pressure apparatus and the chest was opened through the 7th left interspace. The left phrenic was divided as close to the diaphragm as possible, and the left (anterior) vagus trunk was divided about 5 cm. above the diaphragm. The central segment of the phrenic was anastomosed to the distal segment of the vagus by a single atraumatic suture of fine braided silk. All the animals recovered rapidly and uneventfully from this procedure.

In one animal no fistula was prepared, and both phrenics were anastomosed, each to the corresponding vagus, at an interval of one month.

**Collection of Samples.**—Samples of resting secretion were collected once weekly from each animal 18 to 24 hr. after feeding. A catheter with multiple perforations was introduced into the stomach through the fistula. Any secretion present in the stomach, and any produced in the succeeding 15 min., was collected by continuous suction. The volume, *p*H, free and total acid, and pepsin were estimated. The acidity was estimated by electrometric titration, free acid to *p*H 3·5, and total acid to *p*H 8·0. The method of Hunt (1948) was used for the pepsin estimation.

**Terminal Experiments.**—A terminal experiment was carried out on each of the four animals. Anæsthesia was induced with thiopentone and maintained with pentobarbitone. In the first two a combined procedure was attempted, intended : (1) to show that phrenic impulses were passing down the vagus ; (2) to investigate the effect of electrical stimulation of the anastomosed phrenic on the gastric secretion. Attempts were first made to obtain oscillograph recordings from chlorided silver electrodes on fine vagal branches on the anterior gastric wall. After this was completed the pylorus was tied and an œsophageal tube passed into the stomach, which was washed out every 15 min. with 50 ml. N/200 HCl. The washings were titrated with N/20 NaOH and Töpfers indicator and the output of acid/15 min. determined. The anastomosed phrenic was then stimulated in the neck with a Ritchie Snaith stimulator.

In the remaining two animals the recording was done from the chest, artificial respiration being maintained from a pump. The electrodes were applied about 5 cm. below the anastomosis at the point where the vagus trunk broke up into small branches. To facilitate the recording the nerve was cut at this point, and no secretion studies were made.

## HISTOLOGY

At the end of the above procedures the animal was killed and the stomach removed, together with the lower half of the œsophagus and the vagus nerves. The organ was opened along the greater curvature and after careful examination was pinned out, mucosal side downwards, on a large sheet of cork.

Glass rods were placed beneath it to allow free access of the fixative to the mucosa. The nerve-trunks were pinned out under slight tension and the whole was immersed in 5 per cent formol saline and left for twenty-four hours.

At the end of this time a dissection was made of the vagal distribution to the stomach and the specimen was photographed. Suitable portions of the vagal distribution were removed and thoroughly washed in running water for six hours. They were then placed in a 1 per cent solution of osmium tetroxide for forty-eight hours. After removal from this solution they were again washed thoroughly before being dehydrated in increasing grades of alcohol, cleared in chloroform, and embedded in paraffin wax. In the dogs with only the anterior anastomosis, control material was provided from the posterior vagus. Further control material was obtained from three other dogs, the stomachs of which were prepared as above.

In addition to the nerve material, several blocks were cut from each stomach for routine histological examination.

**Counting Technique.**—Our original plan was to demonstrate the success of the anastomoses by making total counts of medullated fibres in the abdominal vagus and its gastric branches in anastomosed and control preparations. We found, however, that in some of the controls the abdominal vagi contained appreciable numbers of small medullated fibres. Although there were significantly more medullated fibres in the anastomosed preparations it appeared that a method of presentation which did not take into account fibre size would not give an adequate impression of the marked difference in appearance between sections of the anastomosed and control material.

The procedure finally adopted was to make counts of all fibres greater than 5 $\mu$ in diameter. The abdominal vagus was found to contain practically no fibres of this size. The phrenic fibres were mostly greater than 5 $\mu$ in diameter. Two effects might be expected to reduce the size of phrenic fibres below the anastomosis, the small neurilemmal tubes into which they were growing (Simpson and Young, 1945), and their failure to establish their proper peripheral connexions (Sanders and Young, 1944). In spite of this about half the medullated fibres below the anastomosis were greater than 5 $\mu$ in diameter.

Two methods of measurement were employed. In the first, counting was done directly from the sections under a microscope fitted with an eye-piece micrometer. In the second, photomicrograph negatives were taken and projected at known scale on to a suitable screen. The second method was mostly used for the large trunks, i.e., phrenic and vagus just below the anastomosis.

## RESULTS

**1. Duration of Experiment.**—Two of the animals with Mann-Bollman fistulæ were sacrificed at the end of 18 and 20 months respectively. The remaining fistula dog and the animal with the bilateral anastomosis were kept for 33 and 34 months respectively.

*Table I.*—Secretion Results on Dog V3

| Experimental Period | Mean wt. in kg. | No. of Collections | Mean vol. in ml. | Acidity No. of Samples in Each Group | | | Mean Pepsin Concentration units/ml. | |
|---|---|---|---|---|---|---|---|---|
| | | | | *p*H > 7 | *p*H 7·3·5 | *p*H < 3·5 | *p*H > 7 | *p*H < 7 |
| Pre-anastomosis | 10·8 | 8 | 5·3 ±0·5 | 6 | — | 2 | 3 | 116 |
| 1–3 months post-anastomosis | 11·1 | 10 | 4·9 ±1·2 | 6 | — | 4 | 12 | 30 |
| 3–6 months post-anastomosis | 12·0 | 12 | 5·6 ±0·9 | 5 | 5 | 2 | 28 | 101 |
| 6–9 months post-anastomosis | 13·3 | 11 | 5·5 ±0·6 | 10 | 1 | — | 5 | 24 |
| 9–12 months post-anastomosis | 12·7 | 9 | 3·7 ±0·8 | 6 | 1 | 2 | 7 | 54 |
| 12–15 months post-anastomosis | 12·9 | 9 | 6·5 ±1·7 | 4 | 3 | 2 | 21 | 104 |
| 15–18 months post-anastomosis | 14·2 | 8 | 3·5 ±1·0 | 6 | 2 | — | 4 | 19 |
| Destroyed at 18 months | | | | | | | | |

**2. General Condition of the Animals.**—All four remained in excellent condition for the whole period of the experiments and continued to gain in weight. The three with unilateral anastomoses showed no sequelæ whatever from this procedure. The animal with the bilateral anastomosis developed marked hypertrophy of the intercostal musculature. The animal tended to become dyspnœic if vigorously exercised, but apart from this seemed to suffer no disadvantage from the loss of its diaphragmatic movement. The Mann-Bollman fistulæ gave no trouble whatever.

**3. Secretion Studies.**—It had been hoped that the first signs of development of function in the anastomosis would be a change in the level of the basal gastric secretion. Pepsin studies were made because it was thought that because of the great importance of the vagus in the control of its secretion early and large changes might be expected in the output of this enzyme.

In practice, no sustained changes were found in the secretion of acid or pepsin suggestive of the establishment of somatic-autonomic connexions. In all three fistula animals the samples collected were most frequently alkaline. Values as high as *p*H 8 were recorded at times from each of the animals. Samples with a *p*H value below 3·5 occurred rarely,

except when some food residue had remained in the stomach or when the animal had picked up and ingested some foreign material during the fasting period prior to collection. All such contaminated samples were rejected.

In view of the negative character of the results they have been presented in an abbreviated form.

The pepsin figures require special mention. Although the samples for pepsin estimation were acidified as soon as possible after collection, the value of the determinations made on samples of juice with an initial *p*H of about 7 is small. In the tables mean figures have been worked out for the pepsin concentration of samples above *p*H 7 and samples below *p*H 7. The main interest of the former is to illustrate that small amounts of pepsin were present in samples collected at a *p*H above neutrality.

*Table II.*—Secretion Results on Dog V5

| Experimental Period | Mean wt. in kg. | No. of Collections | Mean vol. in ml. | Acidity No. of Samples in Each Group | | | Mean Pepsin Concentration units/ml. | |
|---|---|---|---|---|---|---|---|---|
| | | | | *p*H > 7 | *p*H 7-3·5 | *p*H < 3·5 | *p*H > 7 | *p*H < 7 |
| Pre-anastomosis | 8·3 | 7 | 7·1 ±2·5 | 6 | — | — | 5 | — |
| 1–3 months post-anastomosis | 8·6 | 12 | 5·0 ±1·8 | 7 | 4 | 1 | 4 | 24 |
| 3–6 months post-anastomosis | 9·1 | 12 | 7·6 ±1·5 | 9 | 3 | — | 7 | 18 |
| 6–9 months post-anastomosis | 10·9 | 12 | 7·4 ±0·8 | 11 | 1 | — | 4 | 40 |
| 9–12 months post-anastomosis | 12·0 | 12 | 5·5 ±1·6 | 10 | 1 | 1 | 4 | 34 |
| 12–15 months post-anastomosis | 12·4 | 12 | 5·1 ±0·7 | 7 | 5 | — | 7 | 18 |
| 15–18 months post-anastomosis | 12·5 | 10 | 4·1 ±0·9 | 6 | 1 | — | 10 | 8 |
| 18–20 months post-anastomosis | 12·3 | 7 | 5·6 ±1·2 | 6 | — | — | 4 | — |
| Destroyed at 20 months | | | | | | | | |

In *Tables I–III* the duration of this part of the experiment for each dog has been divided up into a number of 3-month periods. For each period is given the mean weight of the animal, the number of successful collections, and the mean volume collected. The number of experiments in each period where the juice had a *p*H value of about 7, between 7 and 3·5, and below 3·5 is also recorded. Although the titratable acidity of each sample was determined, it was felt that little would be added to the above by the calculation of a mean figure for the acidity in each period, and this has not been included.

It will be noticed that the collection of secretion does not continue for the whole post-anastomosis life of the animals. It had been intended to sacrifice the animals shortly after the collections stopped, but delays occurred connected with the transfer of the animals from the Buckston Browne Farm and later with the need to improve the technique of the oscillograph recording.

*Table III.*—Secretion Results on Dog V12

| Experimental Period | Mean wt. in kg. | No. of Collections | Mean vol. in ml. | Acidity No. of Samples in Each Group | | | Mean Pepsin Concentration units/ml. | |
|---|---|---|---|---|---|---|---|---|
| | | | | *p*H > 7 | *p*H 7-3·5 | *p*H < 3·5 | *p*H > 7 | *p*H < 7 |
| Pre-anastomosis | 8·1 | 9 | 8·2 ±1·8 | 3 | 2 | 3 | 16 | 90 |
| 1–3 months post-anastomosis | 8·7 | 10 | 9·2 ±4·6 | 6 | 2 | 2 | 7 | 65 |
| 3–6 months post-anastomosis | 10·0 | 11 | 4·6 ±0·8 | 9 | 2 | — | 16 | 29 |
| 6–9 months post-anastomosis | 10·4 | 12 | 7·1 ±1·2 | 12 | — | — | 4 | — |
| 9–12 months post-anastomosis | 11·3 | 13 | 9·4 ±3·6 | 11 | 2 | — | 3 | 103 |
| 12–15 months post-anastomosis | 11·6 | 11 | 4·0 ±0·8 | 6 | 2 | 2 | 5 | 85 |
| 15–18 months post-anastomosis | 11·5 | 9 | 5·8 ±0·9 | 5 | 3 | 1 | 11 | 24 |
| 18–21 months post-anastomosis | — | 8 | 6·1 ±0·7 | 2 | 4 | — | 1 | 4 |
| Destroyed at 34 months | 14·0 | | | | | | | |

Dog V11, which was prepared with bilateral anastomoses, had no gastric fistula, and therefore no secretion results were obtained. During the 33-month period over which it was maintained, the weight of this animal increased from 8·5 kg. to 13·3 kg.

**Terminal Experiments.**—Our attempts to record phrenic type impulses from small vagal branches on the stomach were uniformly unsuccessful. *Fig.* 135 shows a specimen with the points marked from which recording was attempted. Considerable difficulty was encountered owing to the

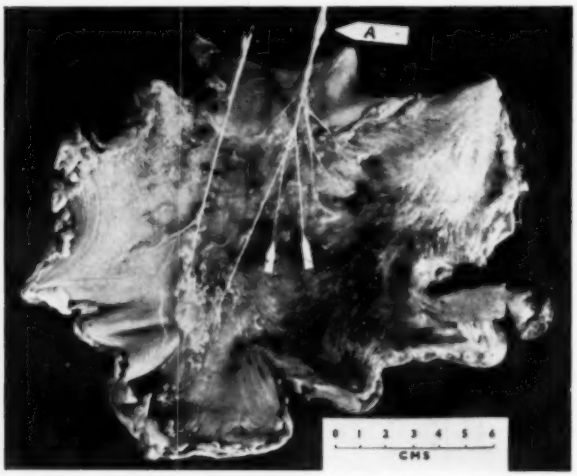



FIG. 135.—Stomach specimen from Dog V5. The anastomosis is clearly visible and the two points from which recording was unsuccessfully attempted are marked by the white arrows. The Mann-Bollman fistula can be seen on the right.

respiratory movement of the stomach and the fact that we did not wish to carry out too much operative interference on the animal, for we hoped to keep it in as good a condition as possible for the stimulation part of the experiment which was to follow. After we had examined histological material from the first two animals in which this was tried, we decided that, although these small branches contained numerous fibres derived from the phrenic, the amount of other tissue around these was such as to render it unlikely that, with the limitations above

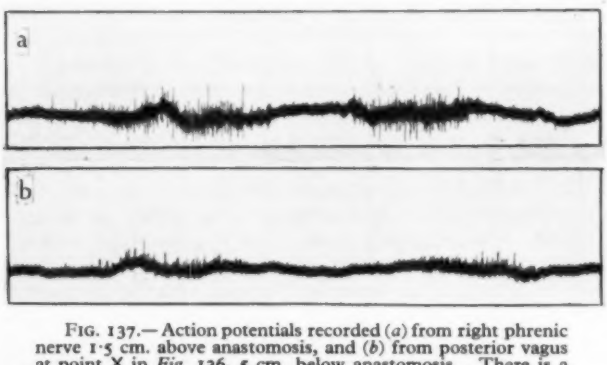



FIG. 137.—Action potentials recorded (*a*) from right phrenic nerve 1·5 cm. above anastomosis, and (*b*) from posterior vagus at point X in *Fig.* 136, 5 cm. below anastomosis. There is a slightly slower respiratory rate in the second record. Slow base-line fluctuations are associated with the mechanical effect of the respiratory movements.

mentioned, we would be able to record satisfactory impulses from them.

We decided that the demonstration that the phrenic impulses were entering the vagal distribution was of greater importance than the attempt to produce secretion in the terminal experiment by electrical stimulation. If such impulses could be demonstrated, then the only point of the stimulation procedure lay in the possibility that the phrenic impulses were of the wrong frequency or duration to excite the vagal terminations. Further, this point in itself could not be definitely established without the evidence that phrenic impulses were actually crossing

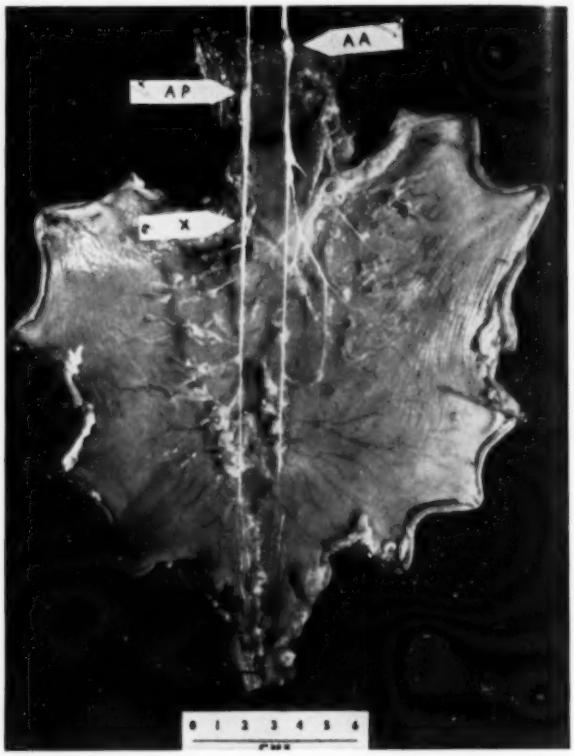



FIG. 136.—Stomach specimen from Dog V11. This animal had bilateral anastomoses. Point X shows the site from which the records shown in *Fig.* 137 were obtained.

the anastomosis. The remaining two animals were therefore devoted entirely to the recording experiment.

Therefore, in the terminal experiments on those two a thoracotomy was performed at the outset. One of these animals was the one with the bilateral anastomosis, and in the other the unanastomosed phrenic was divided. The problems associated with diaphragmatic movement were thus largely eliminated. After carefully cleaning the nerves it was possible in both these animals to pick up phrenic discharges from the anastomosed vagus trunk as far down as the point where it broke up into a number of small branches about 3–5 cm. below the anastomosis. *Fig.* 136 shows the specimen from an experiment in which records were obtained down to the point X and *Fig.* 137 is an example of the record obtained at this point. The discharges below the anastomosis are of less amplitude than above, which correlates with there being fewer fibres of large diameter present in this situation.

**Stimulation.**—Stimulation experiments were performed only in the first two animals sacrificed. The rate of discharge used was 50 impulses per sec., which Heslop (1938) had found most effective for vagal stimulation in cats. Pulse lengths of 1 and 10 sigma were used and a voltage just threshold for

muscle. The anastomosed phrenic was sectioned in the neck and the distal segment was stimulated for periods of up to 30 min. at a time, but no increase in acid or pepsin secretion resulted. We realize that in order to provide an adequate control of the condition of the animals at this stage, secretion should have been demonstrated following stimulation of the opposite normal vagus nerve. This we had intended to do by way of a thoracotomy approach. We had endeavoured to reduce to the minimum the time spent on the recording part of the experiment and had been careful not to interfere with more than two of the small vagal branches on the anterior gastric wall. Unfortunately we tended in each case to spend too long on the stimulation procedure. As we felt that any response found would only be small, we waited for some time to obtain an absolutely steady base-line before stimulation, and we tried more than one period of stimulation at each pulse length. As a result the effect of the further operative procedure in each case was so to impair the condition of the animal that the further stimulation could not be carried out satisfactorily. A rise in secretion was produced in control experiments carried out under similar conditions on two normal dogs, the stimulation now being applied to the distal segments of the vagal trunks which were divided in the chest at a point corresponding to the site of the anastomosis.

**Post-mortem Examination.**—The animals were well nourished. The side of the diaphragm corresponding to the phrenic section was atrophic, and in the one animal with bilateral anastomoses the diaphragm was reduced to a thin membrane save for a small segment anteriorly which was presumably supplied by intercostal nerves.

The anastomoses were surgically satisfactory. Each was represented by a fusiform swelling about 2 cm. in length. They were usually adherent to the œsophagus.

The stomach and abdominal viscera in general showed no abnormality to macroscopical examination.

**Histology.—**

1. *Stomach.*—Several blocks were cut from each stomach, but no histological abnormality was observed.

2. *Nerves.*—The counts of total medullated fibres are shown in *Table IV*. Figures are given only for the phrenics and for the main vagal trunks, control and anastomosed. The corresponding figures for the counts of fibres greater than 5 $\mu$ in diameter are shown for comparison. It will be seen that the anastomosed vagi contain about twice the number of total medullated fibres found in the controls. The difference is much more striking when the count is restricted to fibres greater than 5 $\mu$ in diameter. Practically all the phrenic fibres fall into this group. The control vagi contain almost none, but in the anastomosed vagi nearly half the fibres present are of this size.

The full range of counts of fibres over 5 $\mu$ in diameter which was made to illustrate the spread of phrenic fibres in the distribution of vagal branches on the stomach is shown in the group of outline drawings (*Fig.* 138). Results from three anastomosis dogs and one control animal are illustrated. The neuro-histological material from one anastomosis dog was unfortunately damaged. Such sections as were prepared showed large medullated fibres below the anastomosis, but satisfactory counts could not be made. Two other control dogs showed even fewer fibres of the stipulated size group in the vagal distribution below the diaphragm, and the unoperated vagi in two of the anastomosis dogs form additional control material. These results show clearly that there was good growth of phrenic fibres into the smaller vagal branches on the surface of the stomach. A representative group of photomicrographs illustrating the above is shown in *Fig.* 139, 1–6.

*Table IV.*—DISTRIBUTION OF TOTAL MEDULLATED FIBRES AND OF FIBRES GREATER THAN 5 $\mu$ IN DIAMETER IN THE PHRENIC AND VAGAL TRUNKS IN ANASTOMOSIS AND CONTROL DOGS

| Experiment | Fibre Group | Phrenic | | Normal Vagus | | Anastomosed Vagus | |
|---|---|---|---|---|---|---|---|
| | | Left | Right | Ant. | Post. | Ant. | Post. |
| Anastomosis Dog V5 | Total | 1271 | 1398 | — | 502 | 934 | — |
| | > 5 $\mu$ | 1103 | 1257 | — | 1 | 397 | — |
| Anastomosis Dog V11 | Total | 1236 | 1239 | 528 | — | 1178 | 1246 |
| | > 5 $\mu$ | 1076 | 1159 | 8 | — | 594 | 781 |
| Anastomosis Dog V12 | Total | 1298 | — | — | 339 | 717 | — |
| | > 5 $\mu$ | 1181 | — | — | 1 | 269 | — |
| Control Dog S8 | Total | — | — | 257 | — | — | — |
| | > 5 $\mu$ | — | — | 0 | — | — | — |
| Control Dog S11 | Total | — | — | — | 89 | — | — |
| | > 5 $\mu$ | — | — | — | 0 | — | — |
| Control Dog S17 | Total | — | — | 356 | 449 | — | — |
| | > 5 $\mu$ | — | 1396 | 6 | 1 | — | — |

## DISCUSSION

We make no claim to priority in the idea of applying the technique of phrenic anastomosis to the gastric vagus. Since we began this work we have learned that at least two other groups of workers have in the past carried out limited observations in this field, though they have not completed them to the stage of publication. Ivy, Grossman, and Bachrach (1950) mention two experiments carried out by them in 1920. No evidence of function in the anastomoses was obtained. The survival time of the animals is given only as "several" months.

These writers suggest that the experiment requires repetition.

Jefferson, Necheles, and Phillips (1950) have recently published an account of several phrenic vagus anastomoses in dogs. They investigated effects on motility only, fluoroscopic methods being used during the life of the animals and balloon recording in terminal experiments. The longest observation period was 20 months. No effect suggestive of stimulation of the gastric musculature by respiratory discharges was observed, and no

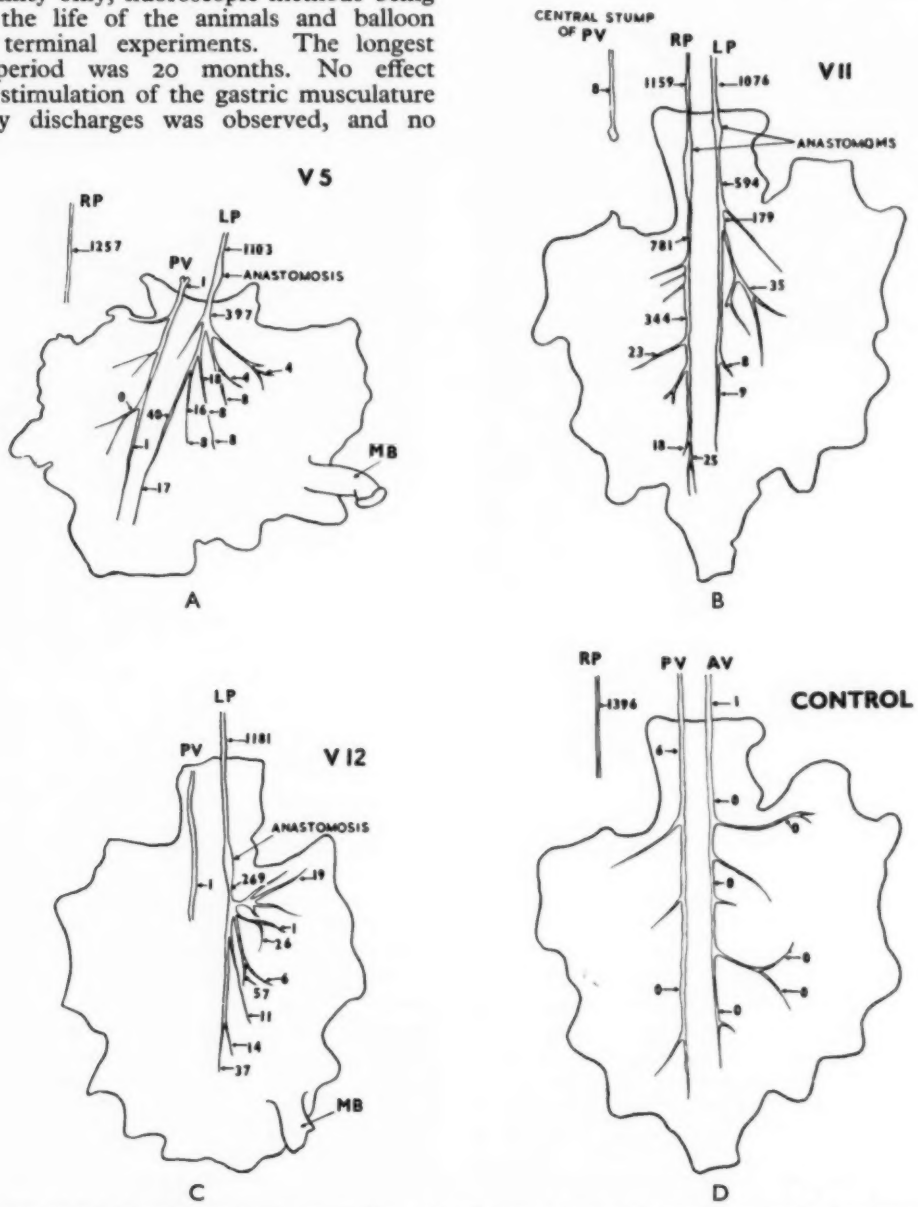
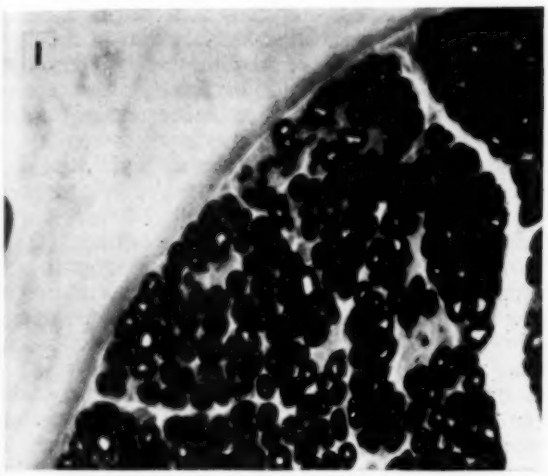
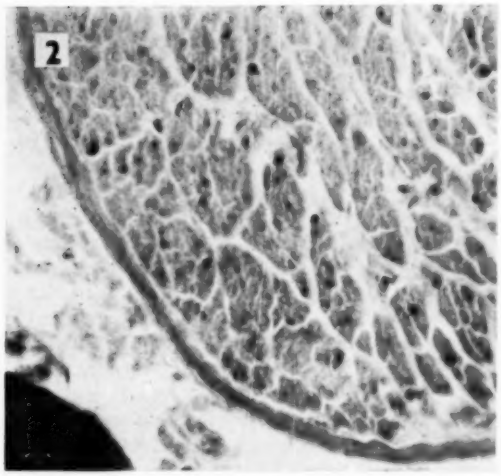
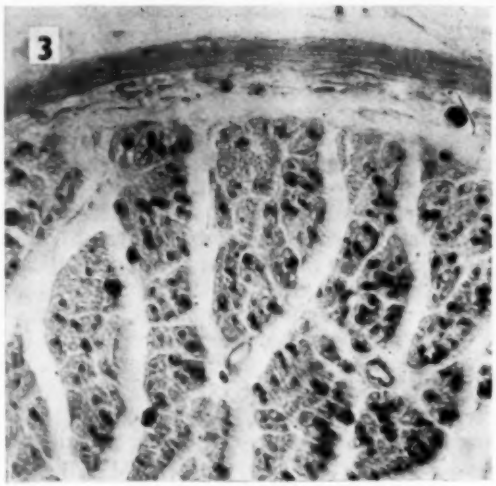


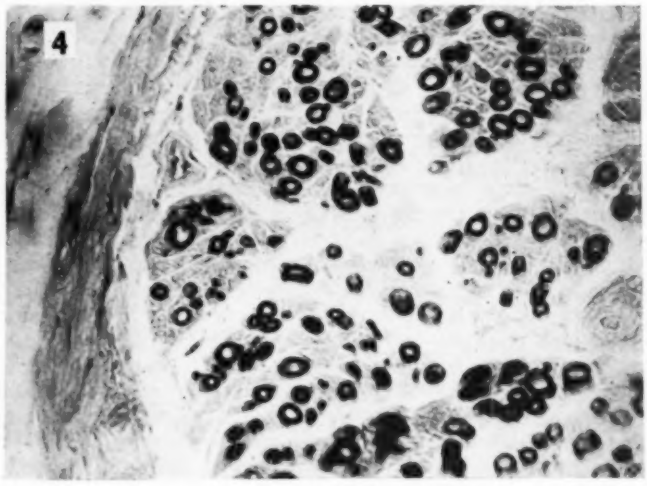

FIG. 138.—Distribution of medullated fibres greater than 5 $\mu$ in diameter in the gastric vagus branches in three dogs with phrenic–vagus anastomosis and one control dog. A, Anastomosis Dog V5. Anterior vagus trunk anastomosed to left phrenic. B, Anastomosis Dog V11. Both vagal trunks anastomosed to corresponding phrenics. C, Anastomosis Dog V12. Anterior vagus trunk anastomosed to left phrenic. D, Control Dog S17. Two other control dogs showed no fibres in this size group in the vagal distribution to the stomach. L.P., Left phrenic; R.P., Right phrenic; A.V., Anterior (left) vagus trunk; P.V., Posterior (right) vagus trunk; M.B., Mann-Bollman fistula.

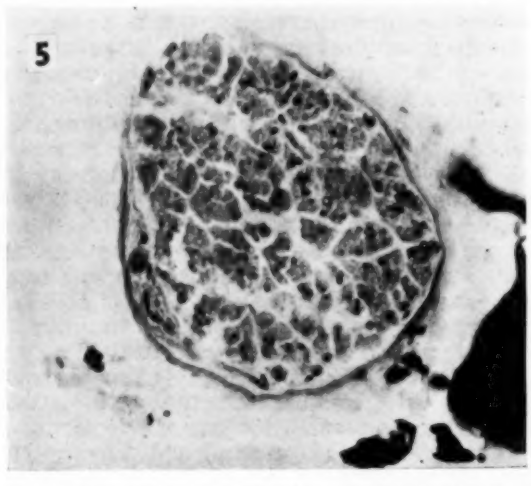
and the effect was only observed when stimulation was applied 2 cm. above the anastomosis. At higher levels on the phrenic no effect was obtained. It is well known in nerve anastomosis work that the results of stimulation below and close above an anastomosis must be interpreted with the greatest caution, since, particularly with autonomic nerves, fibres will travel over large distances from a central stump to re-innervate their old peripheral pathway. That this is true for the vagus nerve has recently been shown by Evans and Murray (1952). They have demonstrated that the regenerating vagus in rabbits will bridge a gap of 2 cm. The fact that these pathological changes were observed in the stomach at post-mortem. Electrical stimulation of the anastomosed phrenic was carried out in terminal experiments on four dogs, and in two of these contraction of the gastric musculature was observed. This is interpreted as demonstrating that "functional" somatic autonomic anastomosis existed. In only one of these two is a full account of the experiment given,



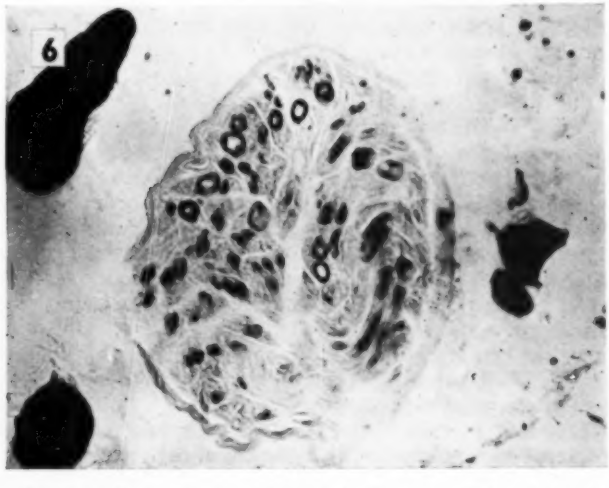




FIG. 139.—1, Portion of phrenic nerve above level of anastomosis; most fibres are greater than 5 $\mu$ in diameter. This and all other specimens were fixed with 5 per cent formol saline before treatment with 1 per cent $OsO_4$. (× 360.) 2, Portion of normal vagus trunk at level of diaphragm; most fibres are non-medullated; a few medullated fibres are to be seen, but these are less than 5 $\mu$ in diameter. (× 360.) 3, Same as 2—a specimen from another animal; this example and that in 2 are both shown in order to illustrate the wide variation in the number of small medullated fibres which can occur. (× 360.) 4, Portion of anastomosed vagus taken from preparation V12 at a site corresponding to the control specimens shown in 2, 3. Many fibres greater than 5 $\mu$ are to be seen. (× 360.) 5, Vagus nerve—taken from a fine branch on the stomach; a few small myelinated fibres may be seen. (× 360.) 6, Similar specimen to that shown in 5 taken from a comparable position in anastomosed preparation V12. Large fibres, greater than 5 $\mu$, are to be seen. (× 360.)

responses to stimulation could not be obtained higher than 2 cm. above the anastomosis appears to us to throw doubt on the possibility that they could have been mediated by phrenic fibres. It seems possible that they could have been the result of spread of the exciting current on to fibres entering the anastomosis derived from the central stump of the corresponding vagus. It is interesting that all four dogs are reported as responding by gastric contraction to stimulation of the vagus nerve below the anastomosis. The writers do not discuss the possibility mentioned above to account for this, but they do suggest that in the two dogs where the anastomoses were shown histologically to be unsatisfactory that the fibres in the left vagus below the anastomosis were derived from the vagus nerve of the right side.

Our experiments show that surgically satisfactory anastomoses between the phrenic and vagus nerves were made. As was expected from previous work on somatic autonomic anastomoses, the phrenic fibres grew into the vagus and spread into its finer branches on the stomach. Phrenic impulses were shown to be crossing the anastomosis. We were not able to trace them into the fine vagal branches, but this was probably due to the difficulties of the recording technique. There seems no reason why, if they were crossing the anastomosis, they should not be conducted to the terminations of the fibres.

No evidence whatever of the production of ulcer was obtained, but neither was there any evidence of the essential prerequisite, i.e., that the fibres should produce functional connexions with the secretory endings of the vagus nerve. Our evidence for the latter statement rests primarily on our failure to observe any changes in the basal secretion of the stomach suggestive of vagal stimulation. The main problem for discussion is whether or not our experiments can be regarded as having provided an adequate test of the possibility of producing such a functional somatic-autonomic anastomosis in this situation. Since the actual anastomoses were surgically satisfactory and conduction was demonstrated across them, our attention must be directed to the terminal connexions.

The first question is whether sufficient time was allowed. With satisfactory suture of the nerve-ends, the delay before fibres appear in the peripheral stump has been estimated by Gutmann, Guttmann, Medawar, and Young (1942) to be of the order of 8 days in the dog. According to the same authors, regenerating somatic axon tips travel down pathways similar to those which they previously occupied at rates of 3–4 mm./day. The distances to be traversed in these preparations were between 10 and 25 cm., so that on the above figures about 100 days should have been adequate for the phrenic fibres to reach even the more remote vagal endings.

It is not certain, however, that fibres growing into very much smaller neurilemmal tubes would maintain rates as high as this. An experiment by Evans (1952) on the rabbit suggests that the rate in these circumstances may be appreciably reduced. The suprascapular nerve was anastomosed to the vagus at the root of the neck. At 120 days a number of medullated fibres had reached the diaphragm, a distance of about 10 cm., but there were many more at 200 days. This suggests that many of these fibres were growing at much slower rates, between 0·5 and 1 mm. a day.

Work on nerve regeneration during the last decade has shown that the arrival of axon tips at the old nerve-endings is not followed by immediate function. A further period is required for the re-establishment of functional connexion, and for maturation of the fibres. This last process involves increase in diameter and degree of myelination, and contact with a suitable end-organ seems to provide the essential stimulus for it to take place (Simpson and Young, 1945; Aitken, Sharman, and Young, 1947). Gutmann and Young (1944), investigating the re-innervation of voluntary muscle, found that the delay was 11 days from the arrival of the fibres when the nerve had been crushed close to the muscle. When the nerve was actually divided and resutured this delay was increased, in some experiments to as long as 55 days. The delay was related to the time taken for the fibres to reach the endings. The increase was apparently due to changes in the motor end-plates during the longer period of atrophy rendering them less susceptible to re-innervation. After very long periods of atrophy only a few muscle-fibres became re-innervated.

The type of preparation under consideration is a very different one from the above, and it might be expected that the delay would be greater when fibres are trying to innervate a type of ending foreign to them. Unfortunately there are no data from experiments on hetero-innervation on which to base a satisfactory estimate of how much time should be allowed for this stage. Previous reports of successful somatic-autonomic anastomoses give neither the distance which the re-innervating fibres had to travel nor the minimum time for function to become possible. The shortest time interval which we have found reported between the surgical preparation of a somatic autonomic anastomosis and a satisfactory test of function is in one of the experiments of Langley and Anderson (1904). Stimulation of the fifth cervical nerve 112 days after it had been anastomosed to the cervical sympathetic in the cat produced well-marked evidence of sympathetic activity on the appropriate side, but how long this response had existed previously is unknown. If we assume that the greater part of this time is represented by this delay at the endings, i.e., about 100 days, and further assume the slowest growth rate discussed above, then the time required to innervate even the most remote endings would be of the order of 600 days. The time allowed in our secretion experiments was of this order, 540, 600, and 630 days in the three dogs, and the last two animals were kept for much longer than this (990 and 1010 days).

Very little work has been done on the hetero-innervation of glandular structures which would throw direct light on to the present problem. An early report by Calugareanu and Henri (1901) describes an experiment in a dog in which the hypoglossal nerve was anastomosed to the lingual above the point where the chorda tympani leaves the latter. After eight months they noticed that the animal showed an increased flow of saliva on feeding, but it was not until 11 months later that they prepared salivary fistulæ and established that the increased flow came from the operated side and that this gland

responded to stimulation of the hypoglossal nerve. A less encouraging recent investigation is that of Evans (1947) on the anastomosis of the peripheral portion of the greater splanchnic nerve to the central end of the first lumbar nerve in rabbits. The animals were maintained for 100–200 days. Hetero-innervation of the adrenal gland occurred, but the pattern was quite abnormal. Fibres penetrated the cortex, which is normally almost devoid of innervation except to blood-vessels, and ended there as large bulbs. In the medulla they failed to form the typical plexuses and ended as large rods. In this paper Evans does not give any evidence of the effect of stimulation, but in a personal communication he reports that no evidence of rise in blood-pressure was produced by stimulation above the anastomosis.

The somatic-autonomic anastomoses which have been quoted have all been somatic to preganglionic autonomic. In spite of the preponderance of non-myelinated fibres in it, the vagus at the diaphragm is regarded by most workers as a pre-ganglionic nerve (Babkin, 1944). The point is important in the present connexion, since we have not seen any reports of functional somatic-postganglionic connexions.

Recently it has been claimed that the vagal innervation to the stomach does not regenerate. Dragstedt, Woodward, and Camp (1950) have found no evidence of return of secretory function as judged by insulin tests for periods of up to three years in dogs with vagus nerve crushes above the diaphragm. It seems that two possibilities might account for this, either failure of the vagus fibres to grow down below the crush, or failure of the fibres to re-establish connexion with their endings. Evans and Murray (1952) have investigated this problem in rabbits. They have shown that the vagal fibres do grow down their old pathways, but at a slower rate than somatic fibres.

It does appear, therefore, that there is no definite evidence at present that the secretory endings of the vagus can be re-innervated even by their normal connexions. Dragstedt and others, however, do rely primarily on the insulin test to demonstrate the return of innervation. Burstall and Schofield (1953) have recently shown that this test is unsatisfactory for the detection of very small degrees of vagal innervation in dogs.

In conclusion, therefore, it appears that there is no definite information as to how long the phrenic fibres might take to establish functional connexions with the secretory endings of the gastric vagus, or indeed that they could effect such connexions at all. The balance of evidence seems against this possibility and suggests that even if such connexions were established the number of vagal endings actually innervated would be small. This last point would very likely vitiate the value of the procedure for the production of gastric hypersecretion. It seems unlikely that any further time could have been profitably allowed in our experiments, since with longer periods of denervation the chances of endings becoming re-innervated decline. Thus although surgically successful conducting anastomoses were prepared, in the absence of any evidence of functional somatic-autonomic connexion no information relating to the causation of peptic ulcer is produced by the experiments.

## SUMMARY

1. In three dogs, previously equipped with Mann-Bollman gastric fistulæ, anastomoses were made about 5 cm. above the diaphragm between the central end of the left phrenic and the distal end of the left (anterior) vagus trunk. A fourth animal with no fistula had bilateral anastomoses.

2. The basal gastric secretion of the three fistula dogs was sampled weekly over periods of 18–21 months. No changes in acid or pepsin secretion suggestive of continuous vagal stimulation were found.

3. The general condition of the animals was excellent and they continued to gain in weight.

4. Two of the fistula animals were sacrificed after 18 and 20 months. Attempts in terminal experiments to record phrenic impulses from fine vagal branches on the stomach did not succeed, probably owing to technical difficulties. There was no gastric secretion on stimulation of the anastomosed phrenic in the neck.

5. The remaining two animals were destroyed at 33 and 34 months. No stimulation was performed, and phrenic-type impulses were recorded from the vagus nerve as far as 5 cm. below the anastomosis where the trunk divides up into small branches.

6. No post-mortem change was found other than diaphragmatic atrophy. The stomachs were histologically normal. Examination of the vagal distribution to the stomach showed that a good growth of phrenic-type fibres was present in the fine branches on the gastric wall in all four dogs.

7. Our experiments provide no evidence of functional connexion between the phrenic fibres and the vagal secretory endings. The question of whether sufficient time was allowed to establish this connexion is discussed, and it is considered that the experiments constitute an adequate test of the possibilities of the method.

8. In the absence of any evidence of functional connexion the experiments provide no evidence relating to the causation of peptic ulcer.

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# *SHORT NOTES OF RARE OR OBSCURE CASES*

## A CASE OF VOLVULUS OF SMALL INTESTINE DUE TO MULTIPLE MESENTERIC CYSTS

BY A. STANDEVEN, HOVE

THE following case is considered sufficiently unusual to merit putting on record.

### CASE REPORT

Mrs. M. S., a housewife aged 31 years, was admitted to hospital complaining of intermittent colicky pain in the central abdomen of four days' duration. She had vomited first twelve hours after the onset of pain, and repeatedly thereafter. On admission, the vomitus was of a fæcal nature and the bowels had not moved since the onset of symptoms. There were no other symptoms and no previous illnesses of note.

FIG. 140.—Showing volvulus of the ileum due to mesenteric cysts. (× ½.)

ON EXAMINATION.—There was some central abdominal distension and slight tenderness. No mass was palpable. Coinciding with each spasm of pain there was a rush of bowel sounds and the diagnosis of low small-intestinal obstruction was made.

AT OPERATION.—Laparotomy was performed through a right lower paramedian incision and revealed a considerable quantity of free blood-stained fluid. The cause of obstruction was volvulus of the lower ileum due to multiple mesenteric cysts (*Fig.* 140). Approximately 2 ft. of the lower ileum with its mesentery and the contained cysts was resected, but one further cyst close to the origin of the superior mesenteric artery was left behind. The anastomosis, end-to-end, was made 6 in. above the ileo-cæcal junction, and the appendix was removed.

Convalescence was uneventful and apart from one attack of abdominal pain, twelve months later, which settled within 48 hours, the patient has remained well.

PATHOLOGICAL REPORT (Dr. L. R. Janes).—"The specimen consists of many cysts filled for the most part with yellowish opaque fluid, situated in the mesentery and subserous coat of the portion of ileum resected. The latter shows an area of mucosa, approximately 1 in. in diameter, which on section is lymphangiomatous. This confirms the lymphatic origin of the larger cysts. The lesion is benign."

### COMMENT

Mesenteric cysts have been recognized since the sixteenth century and over 300 examples have been recorded. Volvulus is one of the recognized complications, but in most cases the cyst has been an isolated one, and the large number of cysts in this case is decidedly rare. The lower ileum is the common site of these cysts.

I am indebted to Mr. J. R. Griffith for permission to treat and publish this case.

# A CASE OF PARAGANGLIOMA WITH METASTASIS TO THE SPINE

By E. A. JACK and J. D. SIM, Edinburgh

MALIGNANT paraganglioma is a sufficiently rare condition to render the following case, presenting several unexpected features, worthy of record. The patient was seen with a pathological fracture of the twelfth dorsal vertebra causing partial paraplegia, and died suddenly from acute circulatory collapse after induction of anæsthesia and injection of hexamethonium bromide. The true diagnosis was unsuspected until it was revealed at post-mortem examination.

## CASE REPORT

The patient was a married woman of 33 years, living abroad. In the eighth month of her second pregnancy, while walking in the garden, she stumbled over a stone and collapsed with severe pain in her back and paralysis of both legs. She had previously complained of aching pain in the back which she attributed to her pregnancy and to a twist while skiing some months before. Almost complete motor paralysis with partial sensory loss and incontinence of urine and fæces was noted for several days. A week later she was delivered of a stillborn fœtus and passed an uneventful puerperium. Incontinence ceased and partial motor recovery occurred. She was then flown to this country, where she was seen five weeks after the onset of paralysis. There was nothing abnormal in her history apart from the backache—no headaches, giddiness, visual disturbance, or digestive upset. Partial motor paralysis of both legs was present with exaggerated tendon reflexes. Sensation was normal. A gibbus presented over the twelfth dorsal vertebra. X-ray examination showed collapse of the body of the twelfth dorsal vertebra, with partial dislocation, the appearance

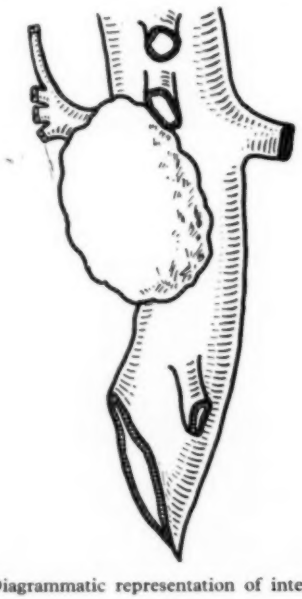

FIG. 141.—Diagrammatic representation of inter-renal tumour.

suggesting a tumour. Clinical examination of heart, lungs, kidneys, breasts, thyroid, and pelvic organs revealed nothing abnormal. Urine contained no abnormal constituents. Blood-picture was normal. B.P. 140/100.

It was decided to perform a laminectomy in the hope of relieving paralysis and obtaining tissue for examination. After induction of anæsthesia with pentothal, cyclopropane was administered and she was given an injection of 40 mg. hexamethonium bromide. Acute circulatory collapse followed almost immediately and, despite all efforts at resuscitation, she died before the operation was started.

AUTOPSY FINDINGS.—At autopsy twenty hours after death an ovoid encapsulated retroperitoneal tumour 3 × 2 cm. was found (*Fig.* 141). It lay somewhat obliquely

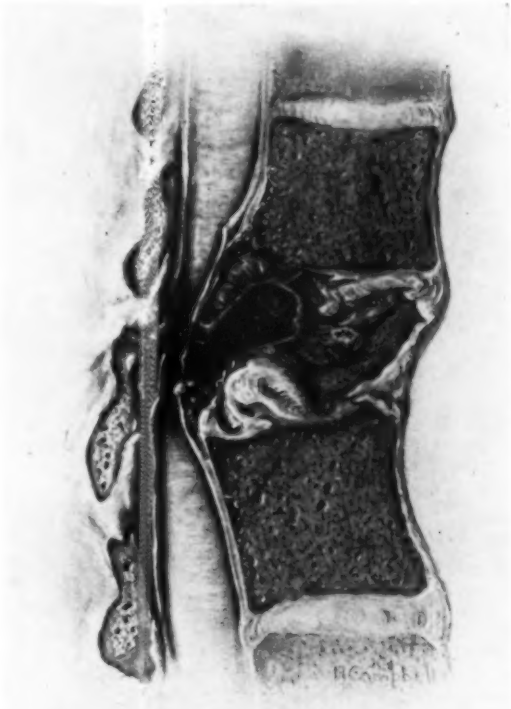

FIG. 142.—Drawing of the secondary tumour in the twelfth dorsal vertebra. A hæmorrhagic cyst lies in the centre of the tumour tissue which is seen encircling the dura and involving the lamina.

with its upper pole anterior to the left renal vessel and reached down to overlap the aorta at the level of the inferior mesenteric artery. On section it was dark red and of fleshy consistence. Anteriorly the capsule was smooth and free, but posteriorly it was bound to the underlying tissues. Both adrenals were normal in position, appearance, and cut section.

The body of the twelfth dorsal vertebra was infiltrated by tumour and had collapsed; the vertebra above was also infiltrated (*Fig.* 142). Tumour tissue had extended into the neural canal and on to the dura at this level. The cord was compressed by tumour tissue extruded from the collapsed vertebral body. No other osseous deposits were found. The skull was opened. No abnormality of the meninges, brain, or cerebral vessels was noted.

The positive findings in the cardiovascular system were a slight but definite left ventricular hypertrophy and dilatation of the right atrium in a heart weighing 320 g. Early patchy atherosclerotic changes were present in the coronary vessels and lower abdominal aorta. Antemortem thrombus, partly organized, was found on the left internal iliac vein. Considerable care was taken to exclude a pulmonary embolus.

The kidneys weighed 120 g. each. Their capsules stripped easily, leaving a smooth surface broken over the

left kidney by a single old depressed scar. Neither the parenchyma nor the vessels presented any notable abnormality on section or on microscopy.

*Microscopy*.—Sections from the inter-renal tumour and from the affected vertebræ were similar. The tissue consisted of loosely grouped oval and polygonal cells in a fine vascular stroma. The nuclei were relatively dense, somewhat variable in size, and well defined, with here and there multinuclear forms. Nucleoli could be made out in many. Mitotic figures were very rare. The cytoplasm was abundant and granular, with indistinct outlines. Scattered areas of hæmorrhage were present (*Fig*. 143). In the vertebral sections widespread infiltration of cancellous and cortical bone by tumour had taken place (*Fig*. 144).

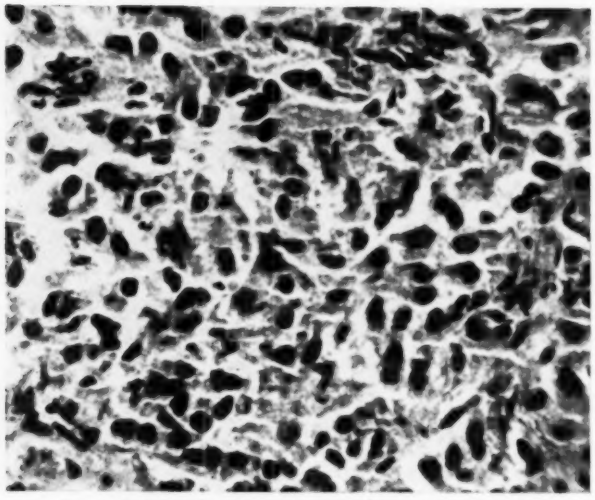

FIG. 143.—Section from inter-renal tumour. Stained hæmatoxylin and eosin. Zenker fixation. (× 380.)

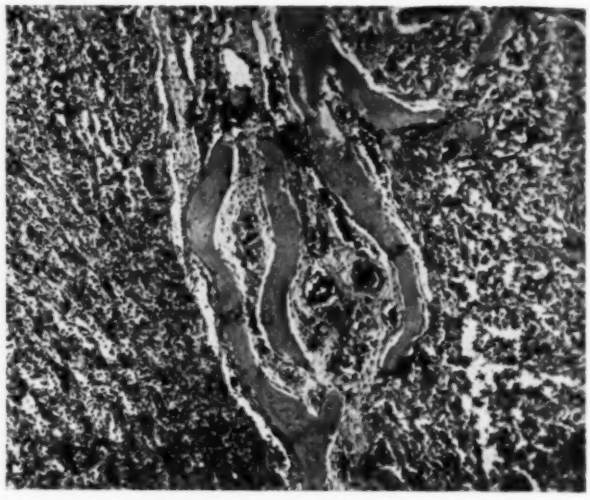

FIG. 144.—Section from secondary tumour in vertebral body. Stained hæmatoxylin and eosin. Zenker fixation. (× 56.)

Tissue fixed in Zenker's solution for 24 hours and stained by hæmatoxylin and eosin presented a fairly coarse golden-brown pigmentation in the cytoplasm. Similar sections gave a negative reaction for cytoplasmic iron deposit. Portions fixed in 5 per cent and others in 10 per cent formol for 48 hours and treated with Schmorl's Giemsa stain failed to show the green pigmentation associated with pro-adrenaline particles.

## TUMOUR ORIGIN

The histology, the positive chrome reaction, and the site place the tumour as a paraganglioma. Paraganglia arise from precursor ectodermal cells of the neural crest. These differentiate to form sympathetic ganglion cells on the one hand and phæochromocytes on the other. Collections of the latter, other than those of the suprarenal medulla, are found early in embryonic life in association with the dorsal surface of the sympathetic ganglia, various viscera, and bilaterally alongside the abdominal aorta (Keibel and Mall, 1910). The largest of these aggregates is the organ of Zuckerkandl situated along the anterolateral surface of the aorta, between the level of the renal vein and the aortic bifurcation. In the neonate they are some 11·6 mm. in length. After birth they atrophy but leave histological evidence of their presence in the adult. These collections were called paraganglia by Kohn (1902), and tumours arising from them have subsequently been termed paragangliomata, while those arising from the adrenal medulla are labelled phæochromocytomata.

Chromaffin tumours are rare, the great majority recorded having arisen from adrenal medulla. Graham (1951) reviewed 207 recorded cases. Paragangliomata are rarer still. The majority in this group arise from the organ of Zuckerkandl. Ortega (1952) reviewed 14 cases recently and added 1 case to the recorded list. The chief interest lies probably in the potential secretory activity. Nine of these cases presented symptoms attributable to their secretion, 4 being diagnosed, the remainder were clinically symptomless. Two cases with metastases have been recorded, one by Halscheidt (1949), in a woman aged 24 years with symptoms suggesting paroxysmal attacks of hypertension, and one by Ortega (1952).

## DISCUSSION

Secretory paragangliomata may afford the clinician the opportunity to diagnose the condition. The tumour tissue may be identified histologically and its secretion confirmed by direct assay or by indirect staining for pro-adrenaline particles. Unfortunately, rapid deterioration takes place after death and Blacklock, Ferguson, Mack, Shafer, and Symington (1947) have stated that staining for pro-adrenaline granules gives unsatisfactory results after a lapse of five hours. The failure to demonstrate adrenaline particles in this case is therefore not surprising. Direct chemical assay was not undertaken.

The remaining findings were mild left ventricular hypertrophy and a resting blood-pressure of 140/100 Hg in a young subject with no evidence of primary renal disease. These, in conjunction with the unexpected fatality under anæsthesia, itself a hazard associated with such tumours, warrant a conviction that the tumour was secretory. No final proof has been obtained.

A further interesting aspect of this tumour lies in its contradictory characteristics. It is well differentiated and of slow growth, yet metastases are present. Ortega's case was similar in its behaviour. As Foulds (1951) pointed out in his analysis of what constitutes malignancy, some tumours assume an

aptitude for dissemination independently of their rate of growth. This appears an example of such behaviour.


## SUMMARY

A case is recorded of paraganglioma of the organ of Zuckerkandl with metastases to the spine.


Thanks are due to Professor A. M. Drennan for permission to publish the pathological details of this case, and to Dr. R. F. Ogilvie for his help and encouragement in preparing the account of it. For the drawings we are indebted to Dr. Nora Campbell.

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# TORSION OF MUCOCELE OF THE APPENDIX CAUSED BY A CARCINOID TUMOUR


By GORDON F. CASSIE

WEST MIDDLESEX HOSPITAL, ISLEWORTH


THE excessive rarity of this case warrants its description and discussion. I have been unable to find a similar case described in the world literature.

Torsion of the appendix is very rare, a fact that is pointed out by the five authors in the British literature each of whom records one case (Payne, 1918; Bevers, 1920; Mallace, 1924; McFadden, 1926; Flatley, 1936). There are eleven records in the world literature each of one case of torsion (Pohl, 1920; Seubert, 1927; Staude, 1929; Rosenfeld, 1931; Schmidt, 1932; Takashima, 1934; Kodama, 1934; Neuffer, 1938; Oravecz, 1938; Schlachter, 1939; Wengen, 1942). One author records two cases (Fevre, 1928). Three papers each describe one case of torsion of a mucocele of the appendix (Quattrocchi, 1934; Lentino, 1946; Manzella, 1945). Moseley (1942) discusses torsion as a possible causative factor in gangrenous appendicitis.

Torsion, mucocele, and carcinoid are all very uncommon affections of the appendix; a combination of all three will obviously be very rare. Some

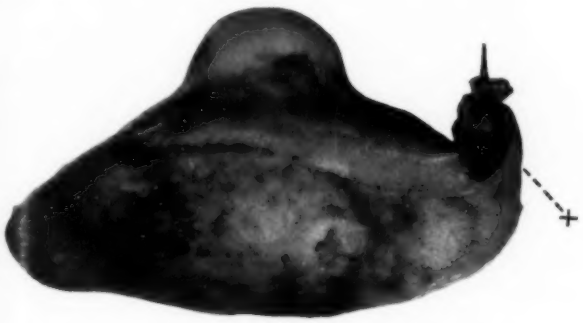

FIG. 145.—The photograph illustrates the size of the specimen and (x) the site of the carcinoid.

idea of this rarity will be gained from the following statements: (*a*) at the New York Post-graduate Hospital only 8 mucoceles were found in 8451 appendices removed at operation (Lentino, 1946); (*b*) Reimann (1918) found only 14 carcinoids in 13,151 appendices excised.

It is significant that most cases of torsion (1) present as a low-grade appendicitis, (2) do not

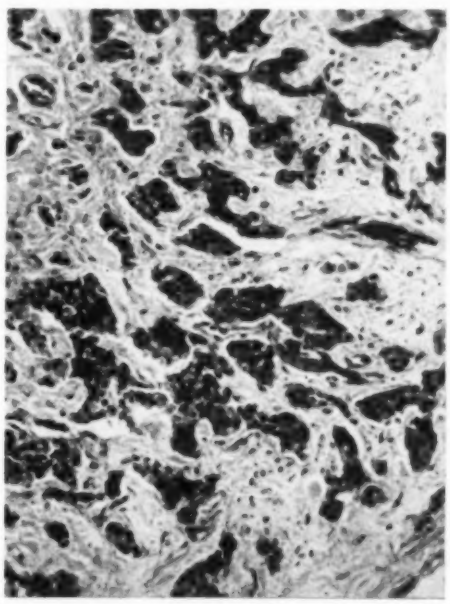

FIG. 146.—The section shows irregularly-shaped masses of spheroidal cells infiltrating a fibrous stroma which occupied the lumen of the appendix.

perforate, (3) occur after the age of 20, (4) have twisted more than once in an anticlockwise direction.

## CASE REPORT

D. M., male aged 25. T. 98·4° F. P. 76.

The patient was referred to the West Middlesex Hospital on July 3, 1952, complaining of continuous right-sided lower abdominal pain for four days after sudden onset, becoming progressively more severe, accompanied by some nausea, constipation, and a little pain on defæcation. He gave no history of previous abdominal pain. On examination, he had a coated tongue, tenderness, and

guarding below McBurney's point. A tender mass could be felt between the upper rectum and the wall of the pelvis on the right side.

OPERATION (July 4).—A right gridiron approach was made and extended downwards in order to deliver intact a tense cystic mass from the right side of the pelvis; this proved to be a large mucocele of the appendix measuring 11 × 6 cm., which had undergone two twists in an anti-clockwise direction. The torsion was undone and appendicectomy performed. The patient was discharged on July 12 after an uneventful convalescence.

THE SPECIMEN.—This was examined carefully and found to have a hard yellow area in the lumen of the appendix at the acute bend just proximal to the mucocele (*Fig.* 145). A fine wedge was cut from this area for section and the histological report (Dr. A. C. Counsell) is as follows: "A severely necrosed carcinoid tumour of the appendix: the lumen of the appendix is occupied by fibrous tissue infiltrated by masses of argentaffin tumour cells. There is no invasion of the appendicular muscle" (*Fig.* 146).

## SUMMARY

A case of torsion of a mucocele of the appendix caused by a carcinoid tumour is presented. The world literature is reviewed and the author has been unable to find any record of a similar case.

My thanks are due to Mr. John Scholefield for his advice, Mr. Vinten for the photograph, and Dr. A. C. Counsell for the histological report and photomicrograph.

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# CARCINOMA DEVELOPING IN CHRONIC OSTEOMYELITIS

BY B. C. ROWLANDS

FIRST ASSISTANT TO THE PROFESSORIAL SURGICAL UNIT OF THE ROYAL INFIRMARY, SHEFFIELD

CARCINOMA developing in the sinuses of chronic osteomyelitis is of infrequent occurrence. Marks and Turner (1950) could find reference to only 83 cases in the literature, to which they added 3 cases of their own. McAnally and Dockerty (1949) found 9 cases of carcinoma in 4000 cases of chronic osteomyelitis which they reviewed at the Mayo clinic, an incidence of 0·23 per cent.

## CASE REPORT

Mrs. G. C., aged 65, was admitted to the Sheffield Royal Infirmary on Feb. 21, 1952.

PREVIOUS HISTORY.—When aged 14 she was operated on for an acute osteomyelitis of the left tibia. The post-operative convalescence she described as being long, with a discharging sinus. After sequestrectomy the sinus healed and she had led a normal life. The sinus broke down and discharged intermittently, never incapacitating her, however, and she never sought medical advice. In 1950 the sinus broke down and had remained unhealed from that date.

RECENT HISTORY.—Two months prior to admission she 'felt her leg crack' while walking, and she had thereafter remained in bed. The sinus developed into a large ulcer with copious and offensive discharge, and which occasionally bled profusely. She had begun to feel weak and complained of dyspnœa.

ON ADMISSION.—Pale; orthopnœic; hæmoglobin 38 per cent.

Overlying the mid-third of the left anterior tibial region was an extensive area of ulceration, irregular in outline, its medial edge being heaped up in a manner suggestive of malignancy. The base of the ulcer consisted of pale, unhealthy-looking granulation tissue. There was a copious foul-smelling sanguineous discharge (*Fig.* 147 A). The limb distal to the lesion was œdematous and movement of the ankle and toes was impossible. There was no clinical evidence of enlarged inguinal glands.

X-RAY EXAMINATION.—This showed general porosis of the bones with a localized area of gross bone destruction in the mid-third of the tibia. In this area there was some increase in diameter suggestive of previous bone reaction (*Fig.* 147 B).

TREATMENT.—Following transfusion the leg was amputated through the thigh. First-intention healing occurred and her general condition improved immediately. To date she remains well, and there is no evidence of metastases.

HISTOLOGY.—Histological examination of a large section demonstrated a well-differentiated squamous-cell carcinoma, which was infiltrating all the tissue shown in the section. The tibia was almost entirely destroyed. (*Figs.* 148, 149.)

## COMMENT

Carcinoma developing in chronic osteomyelitis does so in the cases of long standing where there has been a continual discharge from the sinuses. Both Marks and Turner and McAnally and Dockerty refer to Cohnheim's theory of chronic irritation when discussing the pathogenesis. The first-named authors, however, point out the fallacy of accepting this theory alone in face of the rarity of the condition. They suggest lessening of resistance of the skin in those past middle age and a local reduction of circulation as subsidiary factors. This latter factor may

particularly apply in cases occurring in the lower leg, and Devas (1952), in a recent report, draws attention to the increased incidence of this complication in the tibia.

A B

FIG. 147.—A, Showing large ulcerating area in the anterior tibial region. B, Radiograph showing gross bone destruction in mid-third of tibia.

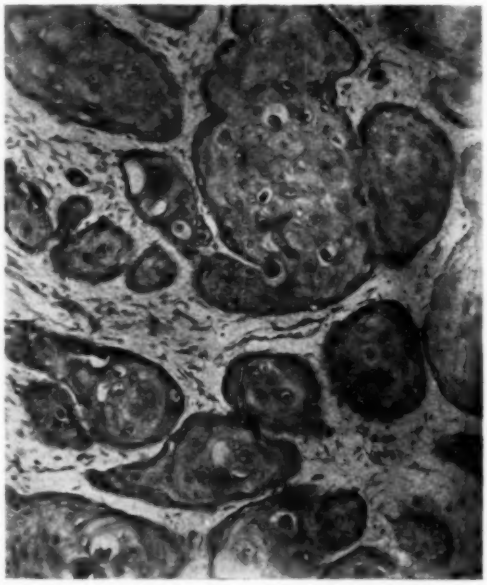

FIG. 149.—Photomicrograph showing the growth to be a typical squamous-celled carcinoma. (× 80.)

In cases where the malignant change is occurring in the deeper recesses of a sinus, clinical recognition may be difficult, but the sudden onset of increased pain, foul discharge, and hæmorrhage is a very suggestive triad of symptoms. When malignancy develops superficially, the external appearances are usually diagnostic, as in this case.

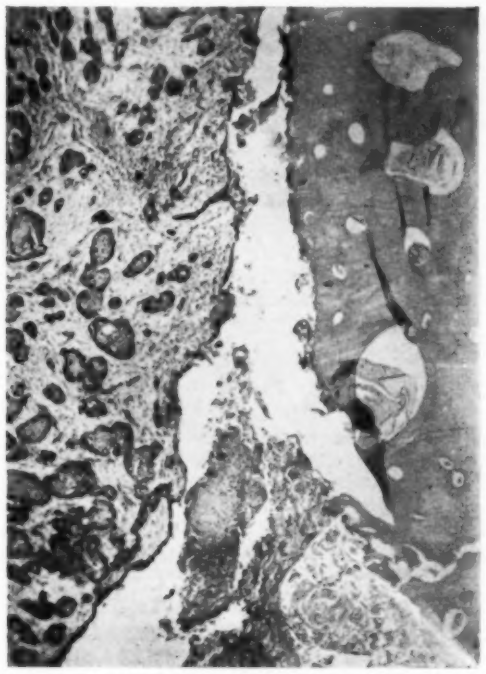

FIG. 148.—Photomicrograph showing a portion of bone surrounded by growth. (× 32.)

The growth is in all cases a squamous-celled carcinoma of a low grade of malignancy. Metastases are infrequent, and all authors comment on the good results of amputation. Enlarged inguinal lymph-glands are not infrequently the result of the usual accompanying mixed infection. If they persist for long after amputation, however, a biopsy should be taken, and if metastases are proved, a block dissection of the whole group considered. In McAnally and Dockerty's series of 9 cases, 2 patients, gland-free at the time of operation, subsequently developed inguinal nodes which were proved by biopsy to be metastases. In the light of this experience, they suggest either block dissection, or irradiation of the groin in all cases as a prophylactic measure.

I wish to thank Professor R. St. Leger Brockman for allowing me to treat and publish this case.

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# CAECOCOLIC INTUSSUSCEPTION FOLLOWING APPENDICECTOMY

By GAVIN CLELAND, M.B.E., Mauchline, Ayrshire

Intussusception following appendicectomy has been reported extremely rarely. Excluding the case now about to be described, it has been possible to find only 5 reports of this condition occurring in the immediate post-operative period. In all these cases operation was for acute appendicitis. A study of this meagre literature reveals a number of points which give considerable food for thought. For this reason it is proposed to describe a personal case and then to review the literature. Thereafter a discussion on the points of interest will be attempted.

## CASE REPORT

A boy, J. R., aged 8 years, was admitted to Seafield Children's Hospital, Ayr, on Feb. 12, 1949, with typical symptoms of acute appendicitis. On the same evening the appendix was removed through a gridiron incision. The base of the appendix was ligated, the stump carbolized and invaginated. The abdomen was closed in layers without drainage. Examination of the appendix showed it to be acutely inflamed at its tip, at which site a pocket of pus was found within the appendix. The proximal portion of the appendix, including its base, appeared quite normal.

For the first three days the post-operative progress was straightforward and the patient had been allowed up. Early in the morning of the fourth post-operative day the boy complained of some pain in the left side, which passed off. However, his appetite was lost. During the day he experienced sudden, short spasms of pain in the epigastrium, which were accompanied by vomiting of watery material on several occasions during the afternoon. Despite several examinations of the abdomen, no definite cause for this pain was found until 8.00 p.m., when the House Surgeon, Dr. A. B. Johnstone, felt a sausage-shaped mass in the epigastrium which ended abruptly at the midline and was felt to the right of the midline. During examination the boy experienced a spasm of pain and at that time the mass was felt to harden. There was no rise in temperature or pulse or respiration rates. Rectal examination showed constipated fæces but no blood. It was impossible to state whether any flatus had been passed.

The House Surgeon came to the conclusion that intussusception was present and, after examination, I agreed with this diagnosis. Accordingly, a laparotomy was planned.

At Operation.—At 9.30 p.m. on the same evening I opened the abdomen through a right lower rectus splitting incision. An intussusception was found extending to half way across the transverse colon. Reduction was easy until the last portion of the intussusception was reached. The cæcum, which appeared to be the apex of the intussusception, was congested and œdematous. As reduction was finally obtained pus was seen to spurt from between the sutures which had been used to invaginate the stump of the appendix. The sutures were removed and the invaginated portion of the cæcum with the base of the appendix was found to form an abscess, with creamy-yellow pus, which had already partially extruded itself in the reduction of the intussusception. As anxiety was felt as to whether the viability of the cæcum in the region of the base of the appendix was adequate, this portion was exteriorized by suture to the parietal peritoneum at the upper end of the laparotomy wound. A rubber drain was placed down to this area and the wound closed in layers apart from the drainage track.

The drain was removed after forty-eight hours and the patient made a straightforward recovery. He was discharged with both operation wounds soundly healed on the eleventh day following the second operation, or fifteen days after original admission.

Table of Findings in 6 Cases of Intussusception following Appendicectomy For Acute Appendicitis

| Author | Age | Sex | Day of Onset after Appendicectomy | Day of Operation after Onset | Tumour Palpated | Rectal Hæmorrhage | Absolute Constipation | Apex of Intussusception | Invagination at Appendicectomy | Pus in Cæcal Wall | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Case* 1 (Broderson) | 28 | M. | 5 | 11 | No | No | No | Base of appendix | Yes | Yes | Survival |
| *Case* 2 (Schaff) | 15 | M. | 5 | 9 | No | No | No | Base of appendix | Yes | Yes | Death |
| *Case* 3 (Roesgen) | 20 | M. | 8 | 9 | Yes | No | ? | Base of appendix | Inferred | Inferred | Survival |
| *Case* 4 (Ingelrans, et al.) | 12 | F. | 3 | 6 | Yes | No | No | Base of appendix | ? | ? | Survival |
| *Case* 5 (Rouquette) | 4 | M. | 12 | Day of onset | ? | No | ? | Base of appendix | Yes | Yes | Survival |
| *Case* 6 (Cleland) | 8 | M. | 4 | Day of onset | Yes | No | Yes | Base of appendix | Yes | Yes | Survival |

## REVIEW OF THE LITERATURE

Similar cases to that now reported have been described by Broderson (1930), Schaff (1933), Roesgen (1943), Ingelrans, Groult, and Loy (1947), and Rouquette (1914). The salient features from these cases, including the one now described, have been tabulated in the accompanying table so that they may be seen at a glance.

Most of the authors point out the extreme difficulty which they experienced in coming to an accurate diagnosis. This is evidenced by the fact that in four of the cases operation for the intussusception was

delayed from one to nine days from its onset. The chief difficulties in the diagnosis appeared to have been the age of the patient, the absence of palpable tumour, the absence of hæmorrhage from the bowel, and the absence of absolute constipation. Of these reasons, the absence of hæmorrhage from the bowel seems to be absolutely constant. The other points are variable or uncertain, depending on the author.

The operative findings are interesting and important. All cases are recorded as presenting with the base of the appendix as the apex of the intussusception. The next important feature is the state of the cæcal wall at the apex of the intussusception. In 4 cases it is stated definitely that an abscess was present in the wall of the cæcum where the base of the appendix had been invaginated. In 1 case abscess is inferred by the author's statement that he believed this to be the cause of the intussusception. In 1 case the cæcal wall in this area is described as being gangrenous. In 1 case there is no definite description. The period of onset following original appendicectomy varies between four days and twelve days after operation. It is also interesting to note that out of the 6 cases now reviewed only 1 death occurred. This is remarkable when it is realized that in one of the surviving cases a delay of eleven days after the onset of intussusception had occurred before operation was carried out.

## DISCUSSION

Save in infants, the commonest cause of a cæcocolic intussusception is probably the existence of a tumour of the cæcum. In the cases now reviewed there would appear to be no fundamental departure from this probability. When the base of the appendix is invaginated into the cæcum, a projection into the cæcal lumen is inevitable. In 3 of the cases this projection was enhanced by the accounts of an abscess around the base of the appendix and the œdema related thereto. Œdema must have been very marked in the case in which gangrene was described.

It should be emphasized at this point that in 5 of the cases invagination of the stump is either actually stated definitely or inferred. The case in which the inference is mentioned is one in which an abscess in the cæcal wall is described. Therefore, it might be suggested that the intussusception would not have occurred if invagination had not been practised in these cases.

Little is to be gained by pursuing this discussion further, save to say that it is remarkable that intussusception does not occur more frequently in view of the artificial manufacture of a projecting tumour by invagination.

One point of significance which emerges is the confirmation of Mayo's remarks (1934). He quoted his pathologist, Dr. Robertson, as stating that in autopsies on patients up to twenty-one days following appendicectomy and dying from a variety of causes, an abscess was found in the cæcal wall at the site of invagination of the stump. Mayo stated that this was one of the reasons why he did not practise invagination of the stump routinely.

Since treating the case described above, I have myself operated upon a patient in whom this intramural cæcal abscess had occurred. This case presented as an acute perforation of an abdominal viscus within ten days of appendicectomy followed by invagination of the appendix stump. At operation, the abscess was found to have burst into the abdominal cavity, and recovery occurred following a stormy convalescence. An entirely similar case was operated upon recently by Mr. Blair A. Thompson, who kindly let me know about it.

The cases discussed present this finding, with the superimposed or resultant intussusception in addition. While no one would dream of suggesting that this tiny group of cases was enough to justify insistence upon a general policy of non-invagination, it may help to strengthen the arm of those who, like myself, only rarely practise invagination of the appendix stump, and then only because of the extreme friability of its base.

## SUMMARY

1. Six cases of cæcocolic intussusception following appendicectomy are discussed. These include one personal case.

2. In all 6 cases the base of the appendix was the apex of the intussusception.

3. In 4 cases invagination of the base had been carried out and an abscess in the resultant cavity in the cæcal wall was present. In 1 additional case this state of affairs is inferred from the author's remarks.

4. Mayo's statement that an abscess of the cæcal wall occurs after stump invagination is further confirmed.

5. The arm of those who do not practise routine invagination of the appendix stump is strengthened.

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ROESGEN, C. W. (1943), *Chirurg*, **15**, 463.
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# *REVIEWS AND NOTICES OF BOOKS*

**Hernia.** A Manual for Truss Fitters. By FRANCIS MITCHELL-HEGGS, T.D., M.B., B.S., F.R.C.S. Consultant Surgeon, Bury and Rossendale Hospital Group. With Forewords by SIR CECIL WAKELEY and Sir CLAUDE FRANKAU. 7¼ × 9¾ in. Pp. 136 + viii, with 97 illustrations. 1953. London: J. & A. Churchill Ltd. 25s.

THIS is an excellent book, and, although it is written primarily for truss fitters, many surgeons will learn a lot about difficult herniæ and the trusses that can be used to keep them reduced.

The illustrations are clear and original, and are reproduced well.

This is a book which students and nurses should read, for they will obtain information that is difficult to obtain elsewhere.

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**The Physician in Atomic Defense.** By THAD P. SEARS, M.D., F.A.C.P., Associate Clinical Professor of Medicine, University of Colorado School of Medicine. With a Foreword by JAMES J. WARING, M.D., M.A.C.P. 5½ × 8 in. Pp. 308, with 53 illustrations. 1953. Chicago: Year Book Publishers Inc. $6.00. (London: Interscience Publishers Ltd. 45s.)

THIS book appears at an opportune time when the world at large is interested in atomic defence. Dr. Sears has written a very readable book in which he reviews the present physical concepts of matter, and discusses radioactivity and its applications. Perhaps the best chapter in the book is that devoted to isotopes, in this Dr. Sears gives a masterly account of the value of isotopes in medicine.

Clinical aspects of atomic warfare are discussed and the management of casualties due to atomic warfare is described.

No doubt this book will do much to stimulate medical thought on atomic warfare and counteract the unrealistic complacency which seems prevalent to-day in both lay and medical minds.

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**Office Orthopædics.** By LEWIS COZEN, M.D., F.A.C.S., Assistant Professor of Orthopædic Surgery, College of Medical Evangelists, Los Angeles. Second edition. 6 × 9¼ in. Pp. 304, with 191 illustrations. 1953. London: Henry Kimpton. 42s.

THE second edition of this small volume on orthopædic surgery has been considerably enlarged and much new matter has been incorporated in the book.

It should supplement the larger works on orthopædic surgery and will be useful to the senior student and house surgeons and casualty officers.

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**An Approach to Clinical Surgery.** By G. H. C. OVENS, O.B.E., M.B., B.S., F.R.C.S., Professor of Surgery, University College of the West Indies. 5¼ × 8 in. Pp. 312 + viii, with 118 illustrations. 1953. London: J. & A. Churchill Ltd. 22s. 6d.

THIS small volume will certainly prove of value to a vast number of students when they enter on their pre-clinical course of studies and seem lost when they leave the dissecting room and enter the wards of a hospital.

Every teaching hospital has an intensive introductory course for the students, and this book covers in a very adequate way the essentials a student requires to know when he is appointed to a surgical firm.

Professor Ovens has written a very useful book.

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**Transactions of the American College of Cardiology.** Vol. II—1952. Edited by BRUNO KISCH, M.D. 6½ × 9¾ in. Pp. 252. Illustrated. 1953. American College of Cardiology. $5.00.

THIS account of the first annual and the fall meeting of the American College of Cardiology is like the reports of most other society meetings in that it contains an interesting and useful selection of articles on various aspects of cardiology. None of them is noteworthy in being original, but all are worth reading.

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**Pathology of Tumours.** By R. A. WILLIS, D.Sc., M.D., F.R.C.P. Professor of Pathology, University of Leeds. Second edition. 6½ × 9¾ in. Pp. 997 + xiv. Index. With 500 illustrations. 1953. London: Butterworth & Co. 84s.

THE first edition of this excellent work appeared in 1948 and was reprinted twice, and now in 1953 a second edition appears; these facts speak for themselves and reveal the popularity of the book.

In the second edition Professor Willis has carefully reviewed the whole of the text, bringing the work completely up to date in the light of the most recent knowledge.

This volume, in our opinion, will prove as useful and as popular as the first edition. A great work which every surgeon will require to possess for ready reference regarding tumours.

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**Hypersplenism and Surgery of the Spleen.** By WILLIAM DAMESHEK, M.D., and C. STUART WELCH, M.D., Pratt Diagnostic Hospital, Boston. 9 × 12 in. Pp. 84 + iv. Illustrated in black and white and colour. 1953. New York: Grune and Stratton, Inc. $10.00.

THIS is a unique volume in many ways; it is an extension of *Spleen and Hypersplenism*, by Dameshek and Estren in 1948, and it is presented in graphic style. The whole eighty pages are held together with plastic rings instead of being bound together as an ordinary book. This method certainly makes for ready reference and the volume lies completely flat no matter at which page it is opened.

The illustrations are beautifully reproduced. The coloured pictures showing the various steps in splenectomy are superb. The modern surgeon is required to have a sound knowledge of splenic diseases and to be able to perform portocaval anastomoses and other vascular shunts. This volume illustrates these particular operations very well indeed. Senior students preparing for higher qualifications in surgery will find this book both useful and interesting.

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**Clinical Methods in Surgery.** By K. DAS, M.B., F.R.C.S. Third edition. Pp. 280 + viii. Calcutta: The City Book Co. 40s.

THIS is the third edition of a students' text-book which is already well known and it is unnecessary to survey it in detail except to notice the changes which have taken

place since the previous edition. Dr. Das has added to most of the descriptions of methods of examining surgical cases an account of the differential diagnosis of the lesions in the various regions and systems under examination, and this constitutes a very valuable addition to the book. The greater part of the work remains, as before, an exhaustive and well-described account of the methods of clinical examination as taught to students of clinical surgery, and it can be recommended strongly both to the students themselves and to junior teachers. The book is profusely and very well illustrated and should form a most valuable addition to every student's library.

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**Surgery of the Pancreas.** By RICHARD B. CATTELL, M.D., and KENNETH W. WARREN, M.D., Surgeons, The Lahey Clinic, New England Baptist Hospital, and New England Deaconess Hospital. 6¾ × 9¾ in. Pp. 374 + xviii, with 100 illustrations. 1953. Philadelphia and London: W. B. Saunders Co. 50s.

THIS book is based on the experience of two surgeons who have treated over 1000 patients with surgical diseases of the pancreas at the Lahey Clinic. This enormous clinical experience gives the authors a real excuse for recording their views on this important subject. Dr. Frank Lahey, whose recent death we all deplore, writes a foreword to this book and warmly recommends it to the surgical profession and states that many new developments will inevitably occur in the surgery of the pancreas but that the views put forward in the book have been founded on experience.

The surgical profession the world over will be delighted with this book, for it is practical in its outlook and clinical acumen is certainly manifested throughout the book.

Perhaps the best part is that devoted to carcinoma of the pancreas; this is of real value to all surgeons who are interested in pancreatic surgery. The details of the various operations are clear and the illustrations are excellent.

This is one of the most important surgical monographs that has so far come from America. We could do with more books of this calibre.

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**Modern Trends in Urology.** Edited by E. W. RICHES, M.C., M.S., F.R.C.S., President, British Association of Urological Surgeons (Home and Overseas); Surgeon and Urologist, The Middlesex Hospital; etc. With a Foreword by the Lord WEBB-JOHNSON, K.C.V.O., C.B.E., D.S.O., T.D., M.B., LL.D., F.R.C.S. 6⅝ × 9⅝ in. Pp. 476 + xiv, with 215 illustrations. 1953. London: Butterworth & Co. (Publishers) Ltd. 75s.

WE have become familiar with Butterworth's *Modern Trends Series* because they are all well written and well produced on good paper. *Modern Trends in Urology* is no exception, in fact, it is one of the best in the series. Mr. Riches has himself an excellent clinical background in urology and has chosen his team of collaborators very carefully. The whole volume is permeated with sound clinical acumen and may be said to represent modern urological methods of treatment both in Great Britain and America. Mr Riches gives an excellent account of the relationship of urology to general surgery and points out the dangers of specialization. Riches also writes on a subject he has made his own—namely, renal neoplasms; this is a beautifully illustrated article.

There are over thirty contributors to this work, each one a specialist in his own subject, and the whole field of urology has been completely covered. Cuthbert Dukes deals with the pathological side, while Whiteside writes on the advances in the radiology of the urinary tract and Bernard Johnson contributes a useful chapter on anæsthesia in urological surgery. Dempster discusses the problems of renal transplantation and rightly states that we want to know many things before renal transplantation will become safe in the human subject. Sir Gordon Gordon-Taylor delights us with an admirable chapter on injuries of the urinary tract in peace and war.

This book will be valued and consulted by both the general surgeon and the urologist. An excellent production.

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**Compression Arthrodesis.** By JOHN CHARNLEY, F.R.C.S. Consultant Orthopædic Surgeon to Manchester Royal Infirmary. Pp. 264 + xi. 1953. Edinburgh and London: E. and S. Livingstone Ltd. 42s.

MR. CHARNLEY has written a very fascinating book in which he reveals the value of compression arthrodesis in the treatment of many joint conditions. There can be no doubt that compression arthrodesis gives persistence of intimate contact and prevents any shearing motion, two important points which have been definitely proved. After excision of the joint the cut bony surfaces are forced together by inserting Steinmann nails above and below the cut surfaces. A compression clamp is attached to either end of the nails and tightened to such an extent with the idea of achieving a load of as near 100 lb. as possible in the case of the knee-joint. Retightening of the clamps during the post-operative period of a month is unnecessary. After a month the pins and clamp are removed and the limb is encased in a groin ankle plaster and full weight-bearing is allowed shortly afterwards. The plaster is removed eight weeks after operation and unprotected weight-bearing permitted.

This certainly is an advance on any other method and Mr. Charnley is to be congratulated on producing a new method of treatment which gives better results in a shorter time.

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**Functional and Surgical Anatomy of the Hand.** By EMANUEL B. KAPLAN, M.D., F.A.C.S., Assistant Professor of Anatomy, College of Physicians and Surgeons, Columbia University. 7 × 10 in. Pp. 288 + xvi, with 132 illustrations. 1953. Philadelphia and London: J. B. Lippincott Co. 80s.

THIS is a well-illustrated monograph in which the functional and surgical anatomy of the hand is discussed in detail. During the last decade several books on the surgery and anatomy of the hand have been published, but none have improved on Wood Jones's classical writings on this subject.

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**A Practice of Thoracic Surgery.** By A. L. D'ABREU, O.B.E., Ch.M., F.R.C.S. 7¼ × 9¾ in. Pp. 591 + viii. Illustrated. 1953. London: Edward Arnold & Co. 80s.

THORACIC surgery is an important branch of surgery and its importance grows almost yearly. This is because many medical conditions in the chest are treated by surgery to-day. During the last decade many advances have been made in the surgery of the thorax and Mr. d'Abreu has incorporated all these in his excellent monograph. He approaches his subject with a very practical clinical background—having served as a general surgeon for several years, he then specialized in thoracic surgery. This valuable experience is demonstrated in this book, which is crammed full of practical details which are so helpful to the reader. The illustrations are numerous and have been well chosen, they are all clear, and help to explain the text in a very definite manner.

The whole book is written in a clear lucid style throughout and this is one of the great advantages of a single author who knows his subject. Multiple authors often make a book disjointed owing to the differences in style of the contributors. Single authorship in a book of this sort means an amazing capacity for work and Mr. d'Abreu certainly possesses this. He is to be congratulated on a work of which British surgeons may well be proud.

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**The Surgery of Infancy and Childhood.** Its Principles and Techniques. By ROBERT E. GROSS, M.D., D.Sc., and WILLIAM E. LADD, Professor of Children's Surgery, The Harvard Medical School; etc. 7 × 10 in. Pp. 1000 + xxiv, with 567 illustrations, the drawings by Etha Piotti. 1953. Philadelphia and London: W. B. Saunders Co. 80s.

THIS large comprehensive volume of one thousand pages deals with every aspect of surgery of infancy and childhood. The principles and techniques of various surgical procedures are well described and the book is lavishly illustrated. As one would expect, a large portion of the book is devoted to the surgery of congenital deformities and this has been performed in an excellent manner.

Some of the pathological tumours of the ovary have new names and one wonders what thecomas and dysgerminomas of the ovary really represent.

Apparently wringer injuries of the arm re very common in America and a separate chapter in the book has been devoted to these injuries. During 1951 142 patients with injuries of this type were admitted to the Boston Children's Hospital. Power-driven washing machines are the cause of this form of injury and the hand and arm of the child is drawn unmercifully into the squeezers and the soft tissues almost invariably sustain considerable damage. One would have thought that a safety device could be installed on these machines to prevent such accidents.

At the end of each chapter a list of modern references is included but these for the most part refer to American writings, very few from other sources are given.

As a book of reference this book could not be bettered for it is exhaustive and completely covers the whole range of children's surgery.

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**The Sulphonamides and Antibiotics in Man and Animals.** By J. STEWART LAWRENCE, M.D. (Edin.), M.R.C.P. Lecturer, Department of Occupational Health, University of Manchester; Out-patient Medical Officer, Salford Royal Hospital, and JOHN FRANCES, M.Sc., M.R.C.V.S., Professor of Preventive Medicine, University of Queensland Veterinary School, Brisbane. Assisted by ARNOLD SORSBY, M.D., F.R.C.S., and PHILIP G. SCOTT, F.R.C.S. 5½ × 8½ in. Pp. 482 + xii, with 39 illustrations. 1953. London: H. K. Lewis & Co. Ltd. 42s.

IT is just seven years since the first edition of this book appeared and during that time many new antibiotics have made their appearance. This second edition should prove of real value to the profession as the chemistry and bacteriology of the various sulphonamides, sulphones, penicillin, streptomycin, and chloromycetin are fully described.

The veterinary chapters by Professor John Francis, of the University of Queensland, are of considerable interest to medical men. Professor Arnold Sorsby contributes an excellent chapter on Eye Diseases while Mr. Philip Scott has revised the Section on Ear, Nose, and Throat Disease.

A very useful book.

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# *BOOK NOTICES*

[*The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.*]

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**Wiederherstellungschirurgie und Traumatologie.** Jahrbuch. Edited by M. LANGE, Bad Tölz, Oberbayern. 6¾ × 9½ in. Pp. 262 + viii. Illustrated. 1953. Basle: S. Karger.

**Chirurgie du Nouveau-né et du Nourrisson.** By BERNAND DUHAMEL, Paris. With a Foreword by MARCEL FEVRE. 6½ × 10 in. Pp. 308, with 158 illustrations. 1953. Paris: Masson et Cie. 1920 Fr.

**The Pluripotency of the Hypophyseal Hormones.** And the Consequences for Endocrinology and Cancerology. By Dr. JULES SAMUELS, Amsterdam. 6¼ × 9½ in. Pp. 296 + xiv. 1953. Amsterdam: N. V. Cycloscoop. G.37.

**Physical Examination of the Surgical Patient.** By J. ENGLEBERT DUNPHY, M.D., F.A.C.S., Assistant Clinical Professor of Surgery, Harvard Medical School; etc.; and THOMAS W. BOTSFORD, M.D., F.A.C.S., Clinical Associate in Surgery, Harvard Medical School; etc. 6½ × 9¼ in. Pp. 326 + xiv, with 188 illustrations. 1953. Philadelphia and London: W. B. Saunders Co. 37s. 6d.

**Surgical Forum.** Proceedings of the Forum Sessions Thirty-eighth Clinical Congress of the American College of Surgeons, New York City, September, 1952. 6¾ × 9¾ in. Pp. 716 + xxxvi. Illustrated. 1953. Philadelphia and London: W. B. Saunders Co. 50s.